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Critical Care [ALERT]

Authoritative, evidence-based summaries for the critical care clinician

SPECIAL FEATURE

Is There a Role for Steroids in ARDS Management?

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

Mortality rates from acute respiratory distress syndrome (ARDS) remain high, even as therapy has improved over the last decade. Recent guidelines for management center on mechanical ventilation, with initial therapy beginning upon identification and treatment of the underlying cause of the ARDS.[1,2] There is reasonable consensus regarding the use of lung-protective strategies, such as low tidal volume ventilation, prone positioning for those meeting criteria for severe ARDS, and restrictive fluid management after the initial resuscitation.[1,2]

However, for patients with the most severe disease, these treatments often are not completely effective, and we look for other therapies that might help. Because ARDS often is a highly inflammatory disease, corticosteroids are suggested frequently as a potential effective treatment modality. Steroids are indicated to treat some of the underlying illnesses that can result in ARDS (e.g., acute eosinophilic pneumonia, community-acquired pneumonia, diffuse alveolar hemorrhage).

Does the current evidence support a role for corticosteroids in the treatment of patients with ARDS for whom the standard guidelines are not effective? If so, when should corticosteroids be used, at what dose, and for what duration?

For years, many investigators have studied the use of corticosteroids in ARDS.[3-6] These authors used modest initial doses of steroids (commonly 1-2 mg/kg/day of methylprednisolone) tapered over about 28 days. (*See Table 1.*) Four of the

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largest trials have been reanalyzed using individual patients' data and a combined trial-level meta-analysis incorporating additional trials in which hydrocortisone was used in early ARDS.[7] Individually, the trials showed improvements in inflammatory markers, ICU length of stay, and ventilator-free days. (*See Table 2.*) In the meta-analysis, the combined trials showed statistically important improvements in some clinically relevant endpoints, including oxygenation, ventilator-free days, and, for those randomized within 14 days of the onset of illness, survival.

However, it has been more difficult to show a consistent mortality benefit overall. While the meta-analysis showed a mortality benefit, the largest trial included in that analysis did not show such a benefit as an individual study. In addition, the meta-analysis included trials with significant differences in study design, such as different primary endpoints, different steroid dose and duration (the most common was 28-32 days), and differences in routine care.

Combined, the studies appear to show an improvement in mortality if steroids are started within the first 14 days of illness. However, there is a suggestion that more rapid tapering of steroids may have resulted in an exacerbation of inflammation-related organ failure and increased adverse outcomes. Also, there is a strong signal from the largest study that starting steroids after 14 days increases mortality.[6]

Several investigators studied the most common steroid-related side effects. They did not find a statistically significant increase in infections or hyperglycemia. The authors of the

Table 1. Randomized Trials of Corticosteroids in Acute Respiratory Distress Syndrome

Study	Number of Patients	Randomization	Initial Methylprednisolone Dose (mg/kg/day)	Duration of Steroids (Days)	Mean Tidal Volume (mL/kg)
Meduri 1998	22	2:1	2	31	10
Rezk 2013	27	2:1	1	28	Not stated
Meduri 2007	91	2:1	1	28	11
Steinberg 2006	177	1:1	1	28	7

Table 2. Outcomes of Randomized Trials of Corticosteroids in Acute Respiratory Distress Syndrome

Study	Inflammatory Markers	Ventilator Days	ICU Length of Stay	Mortality
Meduri 1998	Decreased	Decreased	Not Stated	Decreased
Rezk 2013	Decreased	Decreased	Not Stated	Decreased
Meduri 2007	Decreased	Decreased	Decreased	Decreased
Steinberg 2006	Not Stated	Decreased	Decreased	No effect when started < 14 days Increased when started > 14 days

largest randomized study found an increase in neuromuscular weakness when steroids were started after 14 days.[6] Theoretical concerns remain for other steroid-related side effects, including sodium and fluid retention, which were not addressed in these studies.

There are many different pathways to ARDS. It is a syndrome, not a disease. Many trials use entry and stratification criteria such as PaO_2/FiO_2, which would not be expected to predict a responsive phenotype for any given pharmacologic intervention. The Berlin definition of ARDS has improved our ability to describe the severity of the lung injury, but it doesn't distinguish ARDS due to direct injuries (e.g., pneumonia, inhalation injury) from ARDS due to indirect injuries (e.g., pancreatitis, trauma, non-pulmonary sepsis).[8]

Biological markers are under investigation to define subtypes of patients who might benefit from specific interventions.[9,10] One subtype appears to be hyperinflammatory and hypercoagulable, while the other is hypoinflammatory.

Perhaps agents tested in the past with negative results (e.g., statins, albuterol, growth factors) will be worth reevaluating once a more appropriate subset of ARDS patients with the target phenotype can be identified. We don't necessarily need bigger ARDS trials, just trials with more accurate biological indications and targets for therapy.[11] For now, the role of steroids remains uncertain. Current society guidelines offer conflicting recommendations. Some weakly recommend the use of methylprednisolone at 1-2 mg/kg/day, started within the first 14 days of illness and tapered over at least 28 days. Others do not recommend steroids. High-level vigilance for hyperglycemia, infection, and tight fluid balance are recommended. Moreover, steroids started more than 14 days into the illness increase mortality. Hopefully, the identification of subphenotypes of ARDS patients in the future will allow us to direct these therapies toward patients most likely to benefit from them. ■

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ABSTRACT & COMMENTARY

ICU Bed Availability: Does It Make a Difference?

By Elaine Chen, MD

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

SYNOPSIS: In periods of high medical ICU occupancy, acceptance to the medical ICU may decrease.

SOURCE: Mathews KS, Durst MS, Vargas-Torres C, et al. Effect of emergency department and ICU occupancy on admission decisions and outcomes for critically ill patients. *Crit Care Med* 2018;46:720-727.

Nationwide, the volume of ICU admissions from the ED has increased significantly over recent years (by 50% from 2001 to 2009). When demand exceeds bed availability, complex decisions regarding ICU must be made. Does bed availability affect triage decisions? If many beds are available, patients who are too ill or too well to benefit from the ICU may be admitted. Conversely, if too few beds are available, ICU admission may be denied to patients who may benefit. In prior studies, ICU denial has been associated with increased hospital mortality.

Matthews et al performed this retrospective cohort study of critically ill ED patients to measure the effect of ED crowding and ICU occupancy on ICU admission decisions and to investigate the potential association of delays in admission with in-hospital morbidity and mortality. The setting was a single-center, urban, academic, tertiary care center with a 14-bed closed medical ICU (MICU) that operates at 91% average occupancy. The institution had four additional specialty ICUs to which patients may be admitted as MICU "overflow." The ED had a five-bed high-acuity area.

The patient cohort included all adult ED patients for whom medical ICU admission was requested over a 21-month period. ICU admission began with a request from the ED physicians, followed by an in-person evaluation by the MICU team, and concluded with final decision by the ICU attending physician. Patients "boarded" in the ED until a bed in the admitting unit was available, with the ED team as the primary team for ICU admissions. For patients admitted to an acute care unit, the accepting medical team assumed care while patients still were in the ED. A critical care consult service was available to assist those patients not accepted to an ICU or those in another ICU as "overflow."

The study had two primary objectives: 1) identify whether ED and ICU volume were predictors of ICU admission decisions, and 2) measure

whether post-consult ED boarding time affected in-hospital morbidity (defined as persistent organ dysfunction) and mortality at 28 days. Patient-related characteristics collected included: general demographics, severity of illness scores, timing of consult, primary admission diagnosis, and code status/goals of care at various times. Hospital-related predictors included continuous measurement of ED and inpatient census and overall hospital occupancy. Statistical methods applied included T-test, chi-square, analysis of variance, and multivariable logistic regression. Propensity score methods were used to find factors associated with persistent organ dysfunction and/or death (POD+D).

During this period, there were 854 consults from the ED to the MICU, representing 43.7% of all ICU consults. Overall, 455 patients were accepted to the MICU, with 57 requiring overflow admission. Those who were accepted were younger (mean age, 61 vs. 65 years), were not from nursing homes (12.5% vs. 24.8%), and had higher severity of illness (median mortality probability models scores, 0.15 vs. 0.13). Compared to patients denied admission to the MICU, there were more pulmonary system diagnoses in the accepted group (41.5% vs. 30.8%). There was no association between ED census and admission decision. The MICU often was more full at the time of denial (32.8% of time when patients were denied vs. 25.7% of time when accepted).

Regarding patient outcomes, longer ED boarding time after consult, nursing home origin, and higher initial severity of illness were associated with increased POD+D (i.e., worse outcomes). For those accepted to the MICU, outcomes based on location in the primary MICU or overflow in another ICU were not significantly different (P = 0.44).

In this retrospective cohort analysis, MICU bed availability was found to have a significant effect on the decision to admit critically ill patients in the ED to the ICU, even after adjusting for patient characteristics. This is consistent with other studies that have shown that ICU bed availability affects triage. Longer boarding times in the ED were associated with worse outcomes. Census of other ICUs did not affect admission decisions.

■ COMMENTARY

This study is an interesting evaluation of a single center with a specific admission system from the ED to the MICU. There exist myriad triage models from the ED to ICU and additional models for management of patients who meet ICU criteria when ICU beds are unavailable.

In the model studied, the MICU team evaluates and decides whether patients are appropriate for MICU level of care; the authors found that when the MICU was full, patients had a lower likelihood of acceptance to the MICU. However,

[MICU bed availability was found to have a significant effect on the decision to admit critically ill patients in the ED to the ICU, even after adjusting for patient characteristics.]

census in the other ICUs and ED had no effect on acceptance decisions. This suggests that physicians accounted for, either consciously or subconsciously, the areas of their own work but not necessarily others. The authors evaluated only those patients for whom ICU admission was requested. Were there patients for whom ICU was considered by the ED physicians, but request was not placed? Does ICU census affect ED physicians' request rate? Does acute care census affect the request rate?

When there are no beds available, patients cannot go to them. In this study, patients who experienced a prolonged ED boarding time while waiting for available ICU beds had worse outcomes. This highlights the importance of optimizing throughput and improving care for waiting patients. However, patients admitted to other ICUs staffed by non-MICU physicians with critical care consultation had similar outcomes. This is encouraging, and consistent with prior studies.[1] In my institution, some overflow patients are staffed by medical intensivists, and others are staffed by intensivists trained in other primary backgrounds (such as neurology, surgery, or anesthesia). Could these staffing differences affect outcomes? As with many retrospective cohort studies, this study does not change practice, but challenges our biases and asks questions that may help improve hospital flow. ■

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ABSTRACT & COMMENTARY

An International Survey of Ventilator Weaning Practices

By Betty Tran, MD, MSc, Editor

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

SYNOPSIS: A cross-sectional, multinational survey of adult intensivists revealed significant regional variation in several weaning practices, including screening, weaning modes, techniques to conduct spontaneous breathing trials, the use of written directives, and use of non-invasive ventilation in the peri-extubation period.

SOURCE: Burns KEA, Raptis S, Nisenbaum R, et al. International practice variation in weaning critically ill adults from invasive mechanical ventilation. *Ann Am Thorac Soc* 2018;15:494-502.

The authors of this self-administered, cross-sectional survey of adult intensivists practicing in Canada, India, the United Kingdom, Europe, Australia/New Zealand, and the United States aimed to describe practice variation in several domains related to ventilator weaning. Survey participants were identified via the membership lists for various national critical care societies in set blocks of 300 per region. Participants received postal questionnaires with incentives to participate.

[Although directives for managing sedation were the most commonly used directives across all regions, many respondents reported receiving no written directives to guide care during weaning, particularly regarding managing delirium.]

In total, 1,144 questionnaires were analyzed (Canada, 156; India, 136; United Kingdom, 219; Europe, 260; Australia/New Zealand, 196; United States, 177). Most respondents conducted once-daily screening for patient readiness to wean from the ventilator (70.0-95.6%), although this was reported most frequently in the United States, Canada, and India. Most survey respondents used either pressure support (PS) with positive end-expiratory pressure (PEEP; 56.5-72.3%) or T-piece (off the ventilator; 8.9-59.5%) to conduct a spontaneous breathing trial (SBT). Respondents from India (59.5%) and Europe (45.9%) used T-piece commonly, whereas it was used less frequently in the United States (8.9%), Australia/New Zealand (14.4%), and Canada (21.2%). Although directives for managing sedation were the most commonly used directives across all regions, many respondents reported receiving no written directives to guide care during weaning, particularly regarding managing delirium.

Only about one-third of respondents used the rapid shallow breathing index to decide to proceed with an SBT, and most did not use or consider a cuff leak test. There was significant variation regarding the use of noninvasive ventilation (NIV) for weaning and post-extubation in select subpopulations (e.g., chronic obstructive pulmonary disease, cardiogenic pulmonary edema, etc.).

Finally, there were notable regional differences in who was performing screening (respiratory therapists [RTs] in North America [78.5-87.2%] vs. nurses in the United Kingdom [57.5%] and Australia/New Zealand [44.4%]) and conducting SBTs (RTs in Canada and the United States; attending intensivists and senior trainees in India; and attending intensivists, senior trainees, and nurses in the United Kingdom, Europe, and Australia/New Zealand).

■ COMMENTARY

Current evidence supports several tenets related to ventilator weaning. Protocol-driven screening of patients for ventilator weaning readiness is associated with less time on the ventilator, more

successful weaning, and cost savings.[1,2] Generally, both T-piece and PS are recommended, although the former may underestimate a patient's ability to breathe spontaneously and the latter may overestimate it.[3,4] Multiple trials of SBTs likely are no more successful than once-daily trials.[5] Protocols for ventilator and sedation liberation are recommended, given the associated reductions in duration of mechanical ventilation and/or ICU length of stay.[6]

Despite these recommendations, there is wide regional practice variation among intensivists, as reported in this cross-sectional survey. There are a few interesting findings to note from this study. Academic physicians were well-represented in this survey since survey respondents were identified through membership lists of various critical care societies. As such, there may have been even more practice variation seen if the survey had been extended to other physicians outside of this sampling method.

Second, the regions in which T-piece was employed frequently as an SBT technique (India, Europe) also were regions in which attending intensivists and senior trainees mainly were conducting the SBTs. In contrast, respiratory therapists are more involved in SBT screening and oversight in North America, where written directives on managing sedation, adjusting mechanical support, and conducting SBTs are more likely to be available, but where T-piece SBTs were used less frequently. Monitoring patients on a T-piece SBT tends to be more hands-on given the lack of ventilator alarms; it is unclear whether this variation is due to RT workload (in covering multiple patients off the ventilator on an SBT at the same time) and/or comfort in assessing extubation readiness apart from ventilator data.

Third, although critical care societies recommend written directives to guide care surrounding ventilator weaning, most regions had no directives, especially outside of North America. Finally, these regional differences may be related to broader differences in terms of educational systems and organization, readiness to adopt new practice guidelines, and the presence of external incentives and support; these details are not clear based on this study.

[What will be more important in future studies is the effect, if any, that these regional variations in weaning practices have on actual patient outcomes.]

Overall, the results of this study are enlightening, especially when considering that there are some evidence-based best practice guidelines available concerning ventilator weaning. What will be more important in future studies is the effect, if any, that these regional variations in weaning practices have on actual patient outcomes. ■

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CME/CE QUESTIONS

1. **Corticosteroids increased mortality in acute respiratory distress syndrome (ARDS) when administered after what time in the illness?**
   a. Four days
   b. Seven days
   c. 10 days
   d. 14 days

2. **Which of the following has *not* been observed in trials of corticosteroids in ARDS?**
   a. Increased ventilator-free days
   b. Increased infections
   c. Decreased markers of inflammation
   d. Decreased length of ICU stay

3. **Which of the following findings was described by Mathews et al in their retrospective cohort study of ED and medical ICU (MICU) occupancy?**
   a. When the ED experiences periods of high occupancy, MICU bed requests increase.
   b. When the MICU experiences periods of high occupancy, MICU bed requests increase.
   c. When the hospital experiences periods of low occupancy, MICU acceptance decreases.
   d. ED census has no effect on MICU acceptance rates.

4. **When MICU beds are requested but not accepted or immediately available, which of the following is *true*?**
   a. Patients who experienced extended boarding time in the ED experienced worse outcomes.
   b. Patients who overflowed to non-MICU intensive care units experienced worse outcomes.
   c. Patients who were not accepted to an ICU bed experienced worse outcomes.
   d. Patients who were accepted to an ICU bed exhibited a higher severity of illness.

5. **Based on the survey conducted by Burns et al, which of the following statements is *true*?**
   a. Most respondents conducted a once-daily screening for spontaneous breathing trial (SBT) readiness.
   b. Most respondents used tube compensation to conduct an SBT.
   c. Most respondents reported working from a written directive for managing delirium.
   d. More than 50% of respondents used the rapid shallow breathing index as a criterion for deciding to proceed with an SBT.

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.