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SPECIAL FEATURE

# Improving Sepsis Outcomes: Raising the Bar

*By Kathryn Radigan, MD, MSCI*

*Attending Physician, Division of Pulmonary and Critical Care, Stroger Hospital of Cook County, Chicago*

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

Sepsis remains the leading cause of death in U.S. hospitals.[1] Similar to acute stroke and myocardial infarction, immediate identification and optimal management in the early hours of sepsis improve outcomes. Although we have made strides in the right direction with decreasing mortality rates, the incidence continues to increase.[2] In addition to compliance with the sepsis bundles (now mandated by the United States Centers for Medicare and Medicaid Services), how can critical care providers revolutionize and individualize sepsis care for optimal results?

## HISTORY

Early recognition and appropriate, aggressive treatment have improved sepsis mortality. Early goal-directed therapy (EGDT), as presented by Rivers in 2001, was one of the first studies to bring attention to these issues.[3] Despite some controversy, Rivers was the first to identify high-risk patients, mobilize resources for intervention, and execute a protocol to reverse initial hemodynamic abnormalities associated with sepsis with a subsequent decrease in mortality. After Rivers and his colleagues gained attention, the Surviving Sepsis Campaign (SSC) was launched in 2002 through collaboration between the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine with the goal to reduce sepsis-related mortality. These efforts were advanced further in 2004 when the SSC drafted guidelines for the management of severe sepsis and septic shock, which were updated and optimized in 2008, 2012, and 2016.

## SURVIVING SEPSIS CAMPAIGN GUIDELINES

Although there were a number of adaptations to the 2016 guidelines, initial resuscitation and antibiotics were the focus.[4,5] Strict EGDT targets are no longer emphasized, and dynamic measurements rather than static variables to predict fluid responsiveness are favored. The idea is to use these dynamic variables before and after fluid administration, assessing for

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both fluid responsiveness and clinical improvement. Unfortunately, fluids often are not stopped even when no clinical benefit has been shown.[6] The goal is to transition from a protocolized, quantitative strategy of resuscitation to one that is a more patient-centered approach, guided by hemodynamic assessment, including dynamic variables for responsiveness to fluids and ongoing reevaluation of the patient's response to treatment.

Antibiotics were the other focus, with an emphasis on source control and early, appropriate antibiotics.[4] Although substantial controversy remains, the new guidelines recommend antibiotics targeting the specific source of infection within one hour, with an assessment of whether the patient is at increased risk for resistance and ensuring the antibiotics are dosed optimally. Empiric broad-spectrum therapy with one or more antimicrobials to cover all likely pathogens (bacterial and potentially fungal or viral coverage) for patients presenting with sepsis or septic shock also has been recommended.

## IMPROVING SEPSIS CARE

A multipronged, evidence-based strategy to improve care is recommended. The strategy may include education, sepsis coordinators, early interventions (i.e., antibiotics, fluids, source control), and quality improvement initiatives. Sepsis coordinators and the establishment of a pilot program may be a first step in optimal care. Sepsis coordinators, who act as expert leaders in the field of nursing with critical care experience, are crucial in optimizing sepsis care, identifying barriers, and providing feedback and education in addition to collecting data to institute change in areas that need further development. SCCM guidelines recommend piloting programs on a particular unit, which allows for changes on a small scale, promotes an environment where frontline staff can provide feedback, and ensures that modifications are effective and optimized before a broader initiative to other units.[7]

## EDUCATION

It is vital to develop a system-wide, comprehensive approach to educate all nurses, rapid response teams, physicians, and pharmacists about sepsis. Institutions may start by instituting treatment algorithms and management bundles in accordance with SSC guidelines. Sepsis preference lists and antibiotic algorithms with infusion rates may help to facilitate care and should be available easily or within an order set. Mandatory electronic learning sepsis modules, which include pre-testing, clinical vignettes, and post-testing, have been effective. It is recommended that key information be available online, printed on pocket cards to facilitate wide distribution, and/or posted in all clinical care units and work areas. Educational programs alone have been promising, with one pilot study revealing in-hospital mortality decreased from 79% to 32%, largely as a result of educational efforts by their sepsis program.[8-10]

## EARLY INTERVENTION AND CARE

Earlier identification is achieved more often through a multifaceted approach with nursing as the driving force for the earliest intervention. Usually it starts with the adoption of an institutional surveillance system, screening tool, and/or protocol designed to facilitate early recognition and treatment of sepsis.

Surveillance systems have been widely used for sepsis and often are successful since they are designed to be more proactive rather than reactive in their response to sepsis. These may be manual or automated systemic inflammatory response syndrome (SIRS)-based or non-SIRS-based systems. Although numerous screening tools and protocols are available for use, Thiel and colleagues were some of the first to develop a simple algorithm, the Recursive Partitioning And Regression Tree (RPART) analysis, to generate a prediction model that could be used in an automated fashion to screen hospitalized patients for impending septic shock.[11] Their work revealed a positive predictive value (PPV) of 21.4% and a negative predictive value (NPV) of 96.1% for the diagnosis of septic shock in one of their validation cohorts.[12]

Since that time, multiple electronic algorithms have been developed and improved on these standards. More recently, Churpek and colleagues compared multiple systems for predicting outcomes across different suspicion of infection criteria in hospitalized patients outside the intensive care unit (ICU). The group found electronic

Cardiac Arrest Risk Triage (eCART) to be the most accurate, followed by Modified Early Warning Score (MEWS), the National Early Warning Score (NEWS) system, quick Sequential Organ Failure Assessment (qSOFA), and then SIRS criteria, with SOFA scores found to be the least accurate among both sepsis-specific and general early warning scores.[13] Green and colleagues also revealed the eCART system had superior accuracy in predicting adverse outcomes, including in-hospital cardiac arrest, ICU transfer, and death within 24 hours of observation.[14]

Although standard operating procedures and protocols may appear helpful in optimizing sepsis care delivery, three government-funded, multicenter, randomized, controlled trials from the United States (Protocolized Care for Early Septic Shock [ProCESS]), Australasia (Australasian Resuscitation in Sepsis Evaluation [ARISE]), and the United Kingdom (Protocolised Management in Sepsis [ProMISe]) failed to show lower mortality with EGDT than with usual care.[15-17] Even though protocols have been less successful, compliance with the bundles continues to demonstrate improved outcomes. Levy and colleagues demonstrated that increased compliance with sepsis performance bundles was associated with a 25% relative risk reduction in the mortality rate.[18] Compliance with bundles at 3 and 6 hours and even up to 18 hours have demonstrated a significant mortality benefit.[19,20] Although multiple bundle components of the Sepsis Center for Medicare and Medicaid Services (CMS) Core Measure (SEP-1) were associated with reduced mortality or decreased days of vasopressor therapy for patients who presented with sepsis in the emergency department, only broad-spectrum intravenous antibiotic treatment was associated with reduced mortality when time 0 occurred in an inpatient unit.[21] The most recent severe sepsis bundle recommendations include serum lactate, blood cultures, and antibiotics within three hours, along with 30 mL/kg of crystalloid fluids if evidence of hypotension or elevated lactic acid is present. Repeat lactic acid within six hours is recommended if initial lactic acid is elevated. For septic shock, recommendations are similar but also include a repeat volume status and tissue perfusion assessment, along with vasopressors if indicated, within six hours.

The unfortunate aspect of electronic tools for the identification and treatment of sepsis is that they often are only as good as they are used. Semler and colleagues were involved in a randomized controlled trial that included an electronic tool for the evaluation and treatment of sepsis in the ICU.[22] This electronic tool was built to receive information on patients who met modified SIRS criteria, notify providers of the finding, and solicit an assessment to determine if the patient clinically met criteria for sepsis. Unfortunately, there was no difference between use of the electronic tool and usual care regarding the primary outcome of completion of all indicated SSC six-hour bundle elements or time to completion of each arm individually. There was no difference in ICU mortality, ICU days, and ventilator-free days between the intervention and control groups. This was predominantly because clinicians only used the tool for 28% of available cases. This study emphasizes that the success of future electronic tools to optimize sepsis care depends on clinicians actually using the resources available.

## EARLY ANTIMICROBIAL AND FLUID ADMINISTRATION

As previously mentioned, a recent study showed that broad-spectrum intravenous antibiotic treatment was the only intervention associated with reduced mortality when time 0 occurred in an inpatient unit.[21] Inadequately dosed or delayed antibiotics led to an increased mortality of almost 8% per hour over the first six hours after sepsis diagnosis, supporting the idea that there may be a "golden hour" of antibiotic administration.[23,24] In a multicenter observational study of the timing of antimicrobial administration in septic shock, Amaral and colleagues revealed that patients who were at the highest risk for delays were those admitted to the ICU from the hospital wards, patients in academic institutions, patients with nosocomial infections or pneumonia, and those with longer hospitalizations before the onset of septic shock.[25] Patients who were older, with a higher Acute Physiology Score, more comorbidities, and the absence of fever at presentation also were more likely to have administration of antimicrobials delayed.

For most institutions, it is vital to retrospectively evaluate their own timing of antibiotic delivery and scrutinize for areas of improvement. There may be unacceptably high rates of failure to recognize sepsis or inappropriate empiric antimicrobial initiation (e.g., failure to evaluate previous culture data, evaluate risk factors for resistant organisms, and/or acknowledge previous antibiotic administration).[26] In addition, there may be failure to identify administrative or logistic factors to timely administration. Possible solutions to delays include using "stat" orders, using order sets, addressing delays in obtaining blood and site cultures pending antimicrobial administration, providing optimal sequencing of antimicrobial delivery or using simultaneous delivery of key antimicrobials, as well as improving supply chain deficiencies. Focusing on improved communication among medical, pharmacy, and nursing staff often is most valuable.

Other antibiotic issues also may be due to preparation. If mixing and delivering antimicrobial agents promptly from the pharmacy is not possible, establishing a supply of premixed drugs for urgent situations is a suitable plan of care.[26] If the antimicrobials will not remain stable

as a premixed solution, this issue must be taken into consideration with more troubleshooting. In choosing antibiotics, clinicians should rely on antibiotics safely administered as a bolus or rapid infusion, while others may require an extended infusion. Ensuring prompt IV infusion of antimicrobial agents should be a priority.

The literature on the amount of fluid to administer to patients in septic shock is evolving. While current guidelines recommend a 30 mL/kg crystalloid bolus, this may not apply to patients who have been resuscitated previously. A randomized clinical trial, the Crystalloid Liberal Or Vasopressor Early Resuscitation in Sepsis (CLOVERS) trial, is currently underway and will compare a liberal vs. restrictive approach to intravenous fluid (IVF) resuscitation and earlier use of vasopressors.[27]

## SEPSIS QUALITY IMPROVEMENT INITIATIVES

Armin and colleagues tested a quality improvement initiative that included earlier identification of sepsis, prompt antimicrobial administration, and an educational program. They found a significant improvement in sepsis mortality with an observed sepsis mortality reduction of 4.6%, along with a 1.1-day shorter ICU duration of stay and a 2.2-day shorter overall hospital stay.[28] Although not statistically significant, hospital costs were reduced by $1,949 on average per patient with sepsis.

Levy and colleagues conducted the largest prospective series of severe sepsis patients in more than 30 countries that included a multifaceted, collaborative intervention designed to facilitate adoption of the SSC resuscitation and management bundles. This initiative included physician and nurse champions, introduction of sepsis bundles, education, distribution of a secure database application that allowed for data collection and transfer, as well as audit and feedback.[29] They demonstrated that an increase in compliance with the intervention bundle was associated with a 25% relative risk reduction in mortality. They also observed reductions in ICU and hospital length-of-stay in high-compliance institutions relative to low-compliance institutions.

## SUMMARY

Optimal evidence-based sepsis management includes a multidisciplinary approach with educational interventions, systems for earlier identification, prompt antimicrobial administration, and constant feedback to care teams. It is vital that nurse- and physician-specific barriers to sepsis care are identified and modified. Piloting identified solutions in targeted areas before rolling them out system-wide can provide valuable feedback and other opportunities for optimization. Once these initiatives have been optimized, an institution-specific plan for sustainability of interventions that includes monitoring and feedback is critical. ■

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ABSTRACT & COMMENTARY

# First-Pass Success Rate Between Rocuronium and Succinylcholine in Emergent Out-of-Hospital Endotracheal Intubation

***By Vibhu Sharma, MD, MS***

*Assistant Professor of Medicine, University of Colorado, Denver*

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

SYNOPSIS: This randomized, single-blind, noninferiority trial compared rocuronium and succinylcholine for rapid sequence intubation. Rocuronium was noninferior to succinylcholine with respect to the primary endpoint of first-pass intubation success.

SOURCE: Guihard B, et al. Effect of rocuronium vs succinylcholine on endotracheal intubation success rate among patients undergoing out-of-hospital rapid sequence intubation: A randomized clinical trial. *JAMA* 2019;322:2303-2312.

In the Succinylcholine vs. Rocuronium for Out-of-Hospital Emergency Intubation (CURASMUR) trial, patients requiring intubation were randomized in single-blind fashion to succinylcholine or rocuronium. All patients were intubated outside the hospital by (emergency medicine or anesthesiology) physicians who are part of an advanced ambulance system in France. This system is dispatched to community calls of patients in-extremis, and decisions are made to intubate in the field. The trial enrolled 1,248 patients from January 2014 to August 2018. Consent was obtained either from a relative on site or mailed to the patient after discharge from the hospital or a relative after the patient's death. Most patients were intubated due to coma related to neurologic disease (approximately 50% in each group). Coma due to self-poisoning, acute respiratory failure, trauma, shock, and "other" comprised the rest of the groups, in decreasing order of proportion. Exclusion criteria included known allergies to rocuronium or succinylcholine, known myasthenia gravis, muscular dystrophy, or absence of health insurance. Rocuronium was administered at a dose of 1.2 mg/kg and succinylcholine at 1.0 mg/kg, with patient weights "estimated," although this was not defined. Hypnotics used were either etomidate 0.3 mg/kg or ketamine 2 mg/kg. One-quarter of the patients were intubated while they were on the ground in the field. Interestingly, none were obese, with a mean body mass index (BMI) of approximately 25 in each group. A Macintosh 3 or 4 curved blade was used as the first attempt instrument of choice, with a bougie or laryngeal mask airway (LMA) used for rescue. A video laryngoscope was not used, and reversal of paralysis with sugammadex was permitted, if necessary.

The primary endpoint was first-pass intubation success rate, with secondary pre-specified outcomes including Cormack-Lehane grade view of the cords, overall difficulty of intubation, percentage of patients intubated with an alternative technique, hypoxia, and intubation-related complications (cardiac arrest, arterial hypotension). The majority (98.6%) of the enrolled 1,248 patients completed the trial, and 98.2% completed a per-protocol analysis. The non-inferiority margin was set at 7%. The number of patients with first-pass success in the rocuronium group was 455/610 (74.6%) and in the succinylcholine group was 489/616 (79.4%), with a difference of -4.8% (one-sided 97.5% confidence interval

[CI] -9 to ∞). No differences were noted in the overall intubation difficulty grade or the Cormack-Lehane grade view during direct laryngoscopy. With respect to secondary endpoints, intubation-related complications were more frequent in the succinylcholine group (23.2% vs. 18.2%; $P = 0.04$). Sugammadex had to be used to reverse rocuronium in only two of 610 patients.

## ■ COMMENTARY

This study concludes that rocuronium is noninferior to succinylcholine for intubation in the field and adds to the knowledge about the safety profile of rocuronium. Almost all patients enrolled were able to complete randomization and per-protocol analysis, a fairly remarkable achievement for a community-based trial of this kind. Although no major adverse effects were observed with the use of rocuronium, there were more intubation-related adverse effects (cardiac arrest and hypotension) with the use of succinylcholine. The authors urged caution in the interpretation of the higher rate of cardiac arrest and hypotension in the succinylcholine group; however, it remains true that succinylcholine is associated with numerous adverse effects, including severe hyperkalemia (which can occur within minutes of administration and result in cardiac arrest), while rocuronium is virtually free of adverse effects. The rates of death were equivalent. A higher proportion of patients receiving succinylcholine received post-intubation sedation with opiates and midazolam, presumably related to the shorter duration of action and perceived need for analgosedation in the succinylcholine group.

Some limitations deserve to be highlighted. First, none of the patients were obese; most had a normal BMI (mean ~ 25 in each group) and were intubated in the field. Second, most patients were intubated by experienced emergency medicine physicians and anesthesiologists. For these two reasons, the results of this study cannot be extrapolated to emergency department (ED) or intensive care unit (ICU) settings in the United States or other countries, where patients are intubated by a large variety of clinicians, and patient weights are more varied. Third, the first-pass success rate was lower than is expected in most ED settings[1,2] and may be attributed to the fact that all patients were intubated in the field. Fourth, the noninferiority margin chosen at 7% was set arbitrarily and based on expert opinion. The authors acknowledged this, and cited the lack of randomized trial data as the reason for the arbitrary limit.

The most important conclusion for clinicians who intubate is that rocuronium is safe to use, and the need to reverse the effects should be rare. Intubating conditions and laryngoscopic grade of view are no different with rocuronium compared with succinylcholine in arguably difficult out-of-hospital settings, which should provide a measure of comfort to clinicians who prefer rocuronium in ED and ICU settings. Previous randomized trials[3-5] and more recent large observational studies[1] have demonstrated equivalent intubating conditions with rocuronium and succinylcholine, and this CURASMUR trial adds to the existing literature in this regard. ■

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ABSTRACT & COMMENTARY

# COVID-19 and Steroids: Is There a Consensus on the Controversy?


***By Kathryn Radigan, MD, MSCI***

*Attending Physician, Division of Pulmonary and Critical Care, Stroger Hospital of Cook County, Chicago*

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



SYNOPSIS: A retrospective, single-center cohort study among 201 adults admitted with COVID-19 pneumonia revealed that risk factors associated with the development of acute respiratory distress syndrome (ARDS) and progression from ARDS to death included older age, neutrophilia, organ dysfunction, and coagulation derangement. Treatment with methylprednisolone may be beneficial for these patients.


SOURCE: Wu C, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. *JAMA Intern Med* 2020 Mar 13;e200994. [Online ahead of print].

Researchers continue to scrutinize risk factors for coronavirus disease 2019 (COVID-19). Wu and colleagues performed a retrospective cohort study among 201 adults admitted to Jinyintan Hospital between Dec. 25, 2019, and Jan. 26, 2020, to describe the clinical characteristics and outcomes of COVID-19 patients with pneumonia. Of the 201 patients, 84 (41.8%) developed acute respiratory distress syndrome (ARDS), and approximately half of those died. When compared to non-ARDS patients, ARDS patients complained more often of dyspnea (59.5% vs. 25.6% patients) (difference 33.9%; 95% confidence interval [CI], 19.7% to 48.1%). ARDS patients also had more comorbidities, including hypertension and diabetes. Through bivariate Cox regression analysis, researchers were able to show risk factors associated with ARDS and progression from ARDS to death, which included: older age (hazard ratio [HR] 3.26, 95% CI, 2.08-5.11; HR 6.17, 95% CI, 3.26-11.67, respectively), neutrophilia (HR 1.14, 95% CI, 1.09-1.19; HR 1.08, 95% CI, 1.01-1.17, respectively), and organ and coagulation dysfunction based on higher lactate dehydrogenase (HR 1.61, 95% CI, 1.44-1.79; HR 1.30, 95% CI, 1.11-1.52, respectively) and D-dimer (HR 1.03, 95% CI, 1.01-1.04; HR 1.02, 95% CI, 1.01-1.04, respectively). Although high fever (≥ 39°C) was associated with higher likelihood of ARDS (HR 1.77, 95% CI, 1.11-2.84), it also was associated with a lower likelihood of death (HR 0.41, 95% CI, 0.21-0.82). ARDS patients treated with methylprednisolone had a decreased risk of death (HR 0.38, 95% CI, 0.20-0.72).

The researchers concluded that older age, hypertension, and diabetes are associated with worse outcomes. Although high fever was associated with ARDS development, it also was associated with better outcomes among those patients with ARDS. In addition, treatment with methylprednisolone may be beneficial for patients who develop ARDS.

## ■ COMMENTARY

Learning more about how to treat COVID-19 optimally is not only profoundly important but has reached a state of emergency. COVID-19-related mortality in the United States is progressing rapidly to more than 130,000 patients, and proven treatments are bleak.[1] Shortly after there was evidence that cytokine storm syndrome was associated with the severity of ARDS in COVID-19 disease,[2] corticosteroids became a treatment of great interest, mainly because of their profound anti-inflammatory and immunoregulatory properties. This study is one of the first that references the use of steroids in COVID-19 and boasts that patients with ARDS who are treated with methylprednisolone may be at decreased risk of death.

Of course, these findings and statements must be interpreted cautiously based on this study. The authors openly discussed their concerns that the small sample size and observational nature of the study subject it to potential bias and residual confounding. Furthermore, there also is concern that patients who died in this study population were less likely to be treated with antiviral therapy, and the study does not separate which patients received steroids and/or antivirals. There also is no information on the timing, dosage, or duration of steroids, and whether there were any corticosteroid-related complications observed in the patients who received them.

Although this study is fraught with concerns, the results of the RECOVERY trial, recently announced by press release and now with a published preliminary report, are promising.[3] This study, conducted in the United Kingdom, was a randomized controlled trial that included 2,104 COVID-19 patients given dexamethasone 6 mg once daily by mouth or intravenously for 10 days. When compared to 4,321 patients who received standard care, dexamethasone reduced the death rate in mechanically ventilated patients by 35% and in oxygen-dependent patients by 20% without a benefit in patients who were not receiving respiratory support.

In contrast to the RECOVERY trial, the only other studies available are extremely limited. Another retrospective cohort study by Wang and colleagues, limited to 46 patients, showed that low-dose and short-term methylprednisolone was associated with a shorter time to defervescence along with a more rapid improvement in oxygenation and radiographic abnormalities.[4] Patients on methylprednisolone were weaned off oxygen at a median of eight days vs. 14 days ($P < 0.001$) in the standard of care group. Zhou and colleagues validated the potential benefits of low-dose corticosteroids in a subset of critically ill patients with COVID-19 pneumonia, but interpretation of these data is extremely limited since there were only 15 patients and no control group.[5]

Expert opinion may be used to guide clinicians further but have not been updated since news of the RECOVERY trial. Presently, both the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) recommend that glucocorticoids should not be routinely administered to patients with COVID-19 except in the setting of an evidence-based indication such as asthma or chronic obstructive pulmonary disease exacerbation, refractory septic shock, and adrenal insufficiency.[6,7] In addition to the recommendations by the CDC and WHO, the Society of Critical Care Medicine (SCCM) provides a conditional, weak recommendation in favor of glucocorticoids for the sickest COVID-19 patients who are intubated with severe ARDS ($PaO_2/FiO_2$ ratio < 100).[8] If clinicians choose to administer glucocorticoids, the SCCM suggests that they

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Northwestern University Feinberg School of Medicine
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should begin within the first 14 days, doses should be low, and courses should be short. The Surviving Sepsis Campaign aligns with the SCCM, while the infectious disease guidelines recommend that steroids should be restricted to randomized controlled trials.[9] The initial rationale for not administering glucocorticoids routinely in the COVID-19 ARDS population is that there is evidence of potential harm for patients with other viral pneumonias (i.e., Middle East respiratory syndrome, influenza, and severe acute respiratory syndrome), and the data supporting any benefit did not include a sufficient proportion of patients with viral pneumonia to inform safety.[10-12] In contrast, Fang and colleagues demonstrated that low-dose corticosteroid therapy did not delay viral clearance in COVID-19 patients.[13] It is hoped that keeping the administered dose low also would decrease concerns about secondary bacterial or fungal infections. It will be interesting to observe how these recommendations will be updated once these groups reconvene, and the RECOVERY trial is discussed further.[3] ■

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## CME/CE QUESTIONS

**1. Strategies to improve sepsis care include which of the following?**
a. Education of clinicians
b. Early interventions including antibiotics and source control
c. Quality improvement initiatives
d. All of the above

**2. The goal of the 2016 Surviving Sepsis Campaign Guidelines is to focus on what type of approach guided by assessment of dynamic variables for fluid responsiveness and ongoing reevaluation of the response to treatment?**
a. Patient-centered resuscitation
b. Protocolized resuscitation
c. Quantitative resuscitation
d. Hospital-guided resuscitation

**3. What was the dose of rocuronium used for rapid sequence intubation in the CURASMUR trial?**
a. 0.4 mg/kg
b. 0.6 mg/kg
c. 1 mg/kg
d. 1.2 mg/kg

**4. Which of the following outcomes was more likely to occur with succinylcholine than rocuronium in the CURASMUR trial?**
a. Cardiac arrest or hypotension
b. Intubation difficulty
c. First-pass success for intubation
d. Worse intubation conditions at 60 seconds after drug administration

**5. In the study by Wu et al, it was suggested that the use of methylprednisolone may be beneficial for COVID-19 patients with what concurrent condition?**
a. Acute respiratory distress syndrome
b. Hypercoagulable state
c. Acute renal failure
d. Multiorgan failure

**6. The RECOVERY trial revealed that dexamethasone reduced the death rate by 35% in what population of COVID-19 patients?**
a. Mechanically ventilated patients
b. Hypercoagulable patients
c. Diabetic patients
d. Patients in multiorgan failure