Practice Guidelines

Surviving Sepsis: Updated Guidelines From the Society of Critical Care Medicine

Key Points for Practice

- Avoid the quick Sequential Organ Failure Assessment when diagnosing sepsis because of its inability to accurately rule out patients who will have poor outcomes from sepsis (i.e., low sensitivity). Systemic inflammatory response syndrome criteria, the National Early Warning Score, and the Modified Early Warning Score are more accurate.
- After initial resuscitation with 30 mL per kg of crystalloid fluids, further fluid resuscitation should be based on intravascular volume status and organ perfusion from dynamic measures.
- Empiric antibiotics should be started within one hour in septic shock and within three hours without shock. Empiric coverage for MRSA, gram-negative resistance, or fungal infection is recommended if these pathogens are considered likely.
- High-flow nasal oxygen should be considered to reduce the need for intubation in sepsis-induced hypoxic respiratory failure.

From the *AFP* Editors

Sepsis represents life-threatening organ dysfunction caused by a dysregulated response to infection that kills up to one in three affected people. Early identification and appropriate management can improve these outcomes. The Society of Critical Care Medicine has updated the guidelines of the Surviving Sepsis Campaign.

Identifying Sepsis

Performance improvement programs involving screening programs, education, sepsis bundles, and monitoring for process improvement reduce mortality in patients with sepsis and septic shock with an odds ratio of 0.66 (95% CI, 0.61 to 0.72). Mortality is lower when sepsis bundles are routinely used, at least in high resource countries. Machine learning algorithms are the most accurate way to identify sepsis, with an average 81% sensitivity and 72% specificity.

When using clinical criteria to diagnose sepsis, the quick Sequential Organ Failure Assessment should be avoided because of low sensitivity. The systemic inflammatory response syndrome criteria, National Early Warning Score, and Modified Early Warning Score are more accurate. An early lactate level is recommended if sepsis is suspected because an elevated level correlates with mortality. An elevated lactate level has a positive likelihood ratio of 5 for sepsis, whereas a normal lactate level has a negative likelihood ratio of 0.3.

Resuscitation

With sepsis-induced hypoperfusion or shock, resuscitation with 30 mL per kg of crystalloid fluids is recommended within the first three hours. Failing to meet this initial resuscitation guideline delays resolution of hypotension and increases intensive care duration and mortality.

Balanced crystalloids such as lactated ringers are recommended over normal saline because of weak evidence of decreased mortality. Albumin has no clear benefits over balanced crystalloids and is more expensive. After infusing large volumes of crystalloid fluids, albumin can be considered to improve blood pressure. Hydroxyethyl starch solutions should be avoided because of increased mortality, and synthetic colloid gelatin should not be used because of lack of evidence.

Subsequent resuscitation depends on intravascular volume status and organ perfusion. Static measures such as heart rate, central venous pressure, and systolic blood pressure are poor indicators of fluid status, and using dynamic measures reduces mortality with a risk ratio of 0.59 (95% CI, 0.42 to 0.83). Dynamic measures of fluid status include cardiac output measurement during passive leg raising, stroke volume measurement in response to fluid challenges or changes in intrathoracic pressure, and changes in pulse

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This series is coordinated by Michael J. Arnold, MD, contributing editor.

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CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 494.

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pressure or systolic blood pressure in response to fluid challenges.

Although lactate levels often will not decrease to normal, levels approaching normal suggest successful resuscitation. Normalization of capillary refill time can also demonstrate resuscitation.

If vasopressors are necessary after initial fluid resuscitation, the target mean arterial pressure is 65 mm Hg because higher targets do not improve survival. Vasopressors should be started peripherally rather than waiting for central venous access. Arterial blood pressure monitoring is essential and carries low risks of limb ischemia and bleeding. Intensive care admission should be completed within six hours because mortality increases when emergency department stays exceed that time frame.

Norepinephrine is the first-line vasopressor agent, with epinephrine or dopamine as acceptable alternatives although they increase lactate level and the risk of arrhythmia. Adding vasopressin at 0.03 units per minute should be considered if norepinephrine infusions reach 0.25 to 0.5 mcg per kg per minute without reaching blood pressure goals. Epinephrine can be considered if goals are not met with norepinephrine and vasopressin. For hypoperfusion with adequate volume status and arterial blood pressure, adding dobutamine to norepinephrine or using epinephrine alone are options.

Infection Control

Reducing time to administration of antimicrobials reduces mortality. For patients in septic shock, antimicrobials should be started within one hour because mortality increases with each hour of delay. In sepsis without shock, the evidence is less clear, and antimicrobials are recommended within three hours of recognition. Adding procalcitonin to clinical evaluation for antibiotic initiation does not improve mortality, length of intensive care, or hospitalization and is not recommended.

Because methicillin-resistant *Staphylococcus aureus* (MRSA) accounts for one in 20 infections in critically ill patients, empiric antimicrobial therapy should cover for MRSA in patients at high risk because delays can increase mortality. Although empiric combination antibiotics against gram-negative bacteria do not improve overall mortality, combination antibiotics are recommended for patients at high risk for multidrug-resistant organisms. Similarly, empiric antifungal agents do not improve short-term mortality in critically ill patients but are recommended for patients at high risk for invasive fungal infections.

When beta-lactam antibiotics are used, prolonged intravenous infusions after an initial bolus improve antibiotic concentrations over intermittent boluses and reduce short-term mortality.

Source Control

Controlling the source of infection, including abscess drainage, necrotic tissue debridement, and removing potentially infective devices, is key in management of sepsis. Source control improves survival and is recommended after initial resuscitation.

Ventilation

INITIAL VENTILATORY SUPPORT

In sepsis-induced hypoxic respiratory failure, high-flow nasal oxygen is recommended over noninvasive ventilation because of improved 90-day survival and lower intubation rates. Compared with conventional oxygen, high-flow nasal oxygen reduces intubations but not mortality.

PROTECTIVE VENTILATION

With sepsis-induced acute respiratory distress syndrome (ARDS), low tidal volume ventilation of 6 mL per kg is recommended over higher tidal volumes due to a number needed to treat of 11 to reduce mortality. Similarly, limiting peak airways pressures up to 30 cm of water in ARDS reduces mortality.

Higher positive end-expiratory pressure (PEEP) improves mortality only in moderate or severe ARDS, with an arterial oxygen pressure to inspired oxygen ratio up to 200 mm Hg. PEEP can be titrated to find the lowest driving pressure or to bring plateau airway pressures to 28 cm of water.

In moderate to severe ARDS, prone positioning for more than 12 hours a day within the first 36 hours of intubation improves survival. Prone positioning does not appear to increase life-threatening complications but does increase risk of pressure sores.

As long as light sedation can be maintained, intermittent boluses of neuromuscular blocking agents appear to be safer than continuous infusions.

Venovenous extracorporeal membrane oxygenation reduces mortality in expert centers when mechanical ventilation fails.

Additional Therapies

CORTICOSTEROID THERAPY

In patients with septic shock requiring ongoing vasopressor therapy, intravenous corticosteroids accelerate resolution of shock by 1.5 days and reduce vasopressor requirements without a clear effect on mortality. Typical dosing is hydrocortisone, 200 mg daily, given after four hours of vasopressor therapy as a continuous infusion or every six hours. Corticosteroid use increases neuromuscular weakness.

TRANSFUSION

Because a restrictive transfusion threshold leads to similar mortality as higher thresholds, restrictive transfusions are recommended.

STRESS ULCER PROPHYLAXIS

A proton pump inhibitor for patients with risk factors reduces gastrointestinal hemorrhage without affecting mortality, risk of *Clostridioides difficile* colitis, or risk of pneumonia.

VENOUS THROMBOEMBOLISM PROPHYLAXIS

The risk of venous thromboembolism in critically ill patients may be as high as 14%, and low molecular-weight heparin reduces deep vein thrombosis better than unfractionated heparin and is recommended if possible. Adding mechanical prophylaxis to pharmacologic prophylaxis does not further reduce venous thromboembolism or mortality.

GLUCOSE CONTROL

Because liberal glucose targets lead to similar mortality with reduced hypoglycemia risk, initiating insulin at a serum glucose level of 180 mg per dL (10 mmol per L) or greater and maintaining a target between 144 and 180 mg per dL (8 and 10 mmol per L) should be considered.

VITAMIN C

Vitamin C does not affect mortality in sepsis or septic shock when added to usual care.

SERUM BICARBONATE

Although serum bicarbonate does not improve outcomes in lactic acidosis due to septic shock, it does appear beneficial when severe metabolic acidosis with a serum pH of 7.2 or less occurs with acute kidney injury network score of stage 2 or 3.

Survivor Care

Postcritical illness programs have been developed to address the physical, cognitive, and emotional problems experienced by sepsis survivors but lack evidence of benefit. Physical rehabilitation programs do improve quality of life and reduce depressive symptoms.

The views expressed are those of the author and do not necessarily reflect the official policy or position of the U.S. Navy, Uniformed Services University of the Health Sciences, U.S. Department of Defense, or U.S. government.

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