GUIDELINES FOR MANAGEMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

Surviving Sepsis Campaign


Strength of recommendation and quality of evidence have been assessed using the GRADE criteria, presented in brackets after each guideline. For added clarity:

★ Indicates a strong recommendation or “we recommend”
★ Indicates a weak recommendation or “we suggest”

SSC GUIDELINES HAVE BEEN ENDORSED BY

- American Association of Critical-Care Nurses
- American College of Chest Physicians
- American College of Emergency Physicians
- Canadian Critical Care Society
- European Society of Critical Care Medicine
- European Respiratory Society
- Indian Society of Critical Care Medicine
- International Sepsis Forum
- Japanese Association for Acute Medicine
- Japanese Society of Intensive Care Medicine
- Society of Hospital Medicine
- Surgical Infection Society
- World Federation of Critical Care Nurses
- World Federation of Societies of Intensive and Critical Care Medicine.

Participation and endorsement by German Sepsis Society and Latin American Sepsis Institute.

The Surviving Sepsis Campaign is a collaboration of the European Society of Intensive Care Medicine, the International Sepsis Forum, and the Society of Critical Care Medicine.

Initial resuscitation (first 6 hours)

- Begin resuscitation immediately in patients with hypotension or elevated serum lactate ≥4mmol/L; do not delay pending ICU admission. (★)
- Resuscitation goals: (★)
  - Central venous pressure (CVP) 8–12 mm Hg
  - Mean arterial pressure ≥65 mm Hg
  - Urine output ≥0.5 mL/kg•hr
  - Central venous (superior vena cava) oxygen saturation ≥70%, or mixed venous ≥65%
- If venous O2 saturation target not achieved: (★)
  - consider further fluid
  - transfuse packed red blood cells if required to hematocrit ≥30% and/or
  - dobutamine infusion max 20 μg•kg•min•1
  - A higher target CVP of 12-15 mmHg is recommended in the presence of mechanical ventilation or pre-existing decreased ventricular compliance.

Diagnosis

- Obtain appropriate cultures before starting antibiotics provided this does not significantly delay antimicrobial administration. (★)
  - Obtain two or more blood cultures (BCs)
  - One or more BCs should be percutaneous
  - One BC from each vascular access device in place ≥48 hours
  - Culture other sites as clinically indicated
- Perform imaging studies promptly in order to confirm and sample any source of infection if safe to do so. (★)

Antibiotic therapy

- Begin intravenous antibiotics as early as possible, and always within the first hour of recognizing severe sepsis (★) and septic shock. (★)
- Broad-spectrum: one or more agents active against likely bacterial/fungal pathogens and with good penetration into presumed source. (★)
- Reassess antimicrobial regimen daily to optimize efficacy, prevent resistance, avoid toxicity, & minimize costs. (★)
- Consider combination therapy in Pseudomonas infections. (★)
- Consider combination empiric therapy in neutropenic patients. (★)
- Combination therapy no more than 3-5 days and de-escalation following susceptibilities. (★)
- Duration of therapy typically limited to 7–10 days; longer if response slow, undrained foci of infection, or immunologic deficiencies. (★)
- Stop antimicrobial therapy if cause is found to be non-infectious. (★)

Source identification and control

- A specific anatomic site of infection should be established as rapidly as possible (★) and within the first 6 hours of presentation. (★)
- Formally evaluate patient for a focus of infection amenable to source control measures (eg: abscess drainage, tissue debridement). (★)
- Implement source control measures as soon as possible following successful initial resuscitation. (★)
- Exception: infected pancreatic necrosis, where surgical intervention best delayed. (★)
- Choose source control measure with maximum efficacy and minimal physiologic upset. (★)
- Remove intravascular access devices if potentially infected. (★)

Fluid therapy

- Fluid-resuscitate using crystalloids or colloids. (★)
- Target a CVP of ≥8mmHg (≥12mmHg if mechanically ventilated). (★)
- Use a fluid challenge technique while associated with a hemodynamic improvement. (★)
- Give fluid challenges of 1000 mL of crystalloids or 300–500 mL of colloids over 30 minutes. More rapid and larger volumes may be required in sepsis-induced tissue hypoperfusion. (★)
- Rate of fluid administration should be reduced if cardiac filling pressures increase without concurrent hemodynamic improvement. (★)

Vasopressors

- Maintain MAP ≥65mmHg. (★)
- Norepinephrine or dopamine centrally administered are the initial vasopressors of choice. (★)
- Epinephrine, phenylephrine, or vasopressin should not be administered as the initial vasopressor in septic shock. (★)
  - Vasopressin 0.03 units/min may be subsequently added to norepinephrine with anticipation of an effect equivalent to norepinephrine alone.
- Use epinephrine as the first alternative agent in septic shock when blood pressure is poorly responsive to norepinephrine or dopamine. (★)
- Do not use low-dose dopamine for renal protection. (★)
- In patients requiring vasopressors, insert an arterial catheter as soon as practical. (★)

Inotropic therapy

- Use dobutamine in patients with myocardial dysfunction as supported by elevated cardiac filling pressures and low cardiac output. (★)
- Do not increase cardiac index to predetermined supranormal levels. (★)
Steroids
- Consider intravenous hydrocortisone for adult septic shock when hypotension responds poorly to adequate fluid resuscitation and vasopressors. (1B)
- ACTH stimulation test is not recommended to identify the subset of adults with septic shock who should receive hydrocortisone. (1B)
- Hydrocortisone is preferred to dexamethasone. (1B)
- Fludrocortisone (50 µg orally once a day) may be included if an alternative to hydrocortisone is being used which lacks significant mineralocorticoid activity. Fludrocortisone is optional if hydrocortisone is used. (1C)
- Steroid therapy may be weaned once vasopressors are no longer required. (1B)
- Hydrocortisone dose should be ≤300mg/day. (1A)
- Do not use corticosteroids to treat sepsis in the absence of shock. (1A)

Recombinant human activated protein C (rhAPC)
- Consider rhAPC in adult patients with sepsis-induced organ dysfunction with clinical assessment of high risk of death (typically APACHE II ≥ 25 or multiple organ failure) if there are no contraindications. (2B, 3C for post-operative patients)
- Adult patients with severe sepsis and low risk of death (eg: APACHE II 120 or one organ failure) should not receive rhAPC. (1B)

Blood product administration
- Give red blood cells when hemoglobin decreases to 117.0 g/dL (1120 g/L) to target a hemoglobin of 7.0 – 9.0 g/dL in adults. (1B)
  A higher hemoglobin level may be required in special circumstances (eg: myocardial ischemia, severe hypoxemia, acute hemorrhage, cyanotic heart disease, or lactacidosis).
- Do not use erythropoietin to treat sepsis-related anemia. Erythropoietin may be used for other accepted reasons. (1B)
- Do not use fresh frozen plasma to correct laboratory clotting abnormalities unless there is bleeding or planned invasive procedures. (1B)
- Do not use antithrombin therapy. (1B)
- Administer platelets when: (1C)
  - counts are ≤<br>000/mm³ (5 < 10³/mm³) regardless of bleeding.
  - counts are ≤<br>000/mm³ (5 < 10³/mm³) and there is significant bleeding risk.
  - Higher platelet counts ≥<br>000/mm³ (50 < 10³/mm³) are typically required for surgery or invasive procedures.
- Use a pulmonary artery catheter for the routine monitoring of patients with ALI/ARDS. (1A)
- Use a conservative fluid strategy for patients with established ALI who do not have evidence of tissue hypoperfusion. (1C)
- Avoid neuromuscular blockers where possible. Monitor depth of block with train-of-four when using continuous infusions. (1B)

Sedation, analgesia, and neuromuscular blockade in sepsis
- Use sedation protocols with a sedation goal for critically ill mechanically ventilated patients. (1B)
- Use either intermittent bolus sedation or continuous infusion sedation to predetermined end points (sedation scales), with daily interruption/lightening to produce awakening. Re-titrate if necessary. (1B)
- Provide stress ulcer prophylaxis using H2 blocker or proton pump inhibitor. Benefits of prevention of upper GI bleed must be weighed against the potential for development of ventilator-acquired pneumonia. (1C)
- Discuss advance care planning with patients and families. Describe likely outcomes and set realistic expectations. (1C)

Mechanical ventilation of sepsis-induced acute lung injury (ALI)/ARDS
- Target a tidal volume of 6mL/kg (predicted) body weight in patients with ALI/ARDS. (1B)
- Target an initial upper limit plateau pressure ≤<br>0 cmH₂O. (1A)
- Consider chest wall compliance when assessing plateau pressure. (1A)
- Allow PaCO₂ to increase above normal, if needed, to minimize plateau pressures and tidal volumes. (1C)
- Provide positive end expiratory pressure (PEEP) should be set to avoid extensive lung collapse at end expiration. (1A)
- Consider using the prone position for ARDS patients requiring potentially injurious levels of FiO₂ or plateau pressure, provided they are not at risk from positional changes. (1A)
- Noninvasive ventilation may be considered in the minority of ALI/ARDS patients with mild-moderate hypoxic respiratory failure. The patients need to be hemodynamically stable, comfortable, easily arousable, able to protect/clear their airway, and expected to recover rapidly. (1B)
- Use a weaning protocol and a spontaneous breathing trial (SBT) regularly following stabilization in the ICU. (2B, 2C for post-operative patients)
- Use a mechanical prophylactic device, such as compression stockings, for patients who are at very high risk for DVT. (1A)
- Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for DVT. (1C)
- Use either low-dose unfractionated heparin (UFH) or low-molecular weight heparin (LMWH), unless contraindicated. (1A)
- Use a conservative fluid strategy for patients with established ALI who do not have evidence of tissue hypoperfusion. (1C)
- Use a mechanical prophylactic device, such as compression stockings, for patients who are at very high risk for DVT. (1A)
- Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for DVT. (1C)
- In patients at very high risk LMWH should be used rather than UFH. (1C)
- Use IV insulin to control hyperglycemia in patients with severe sepsis following stabilization in the ICU. (1B)
- Aim to keep blood glucose 118.3 mmol/L (150 mg/dL) using a validated protocol for insulin dose adjustment. (1C)
- Provide a glucose calorie source and monitor blood glucose values every 1-2 hours (4 hours when stable) in patients receiving intravenous insulin. (1C)
- Interpreting low glucose levels obtained with point of care testing, as these techniques may overestimate arterial blood or plasma glucose values. (1C)
- Intermittent hemodialysis and continuous veno-venous hemofiltration (CVVH) are considered equivalent. (1B)
- CVVH offers easier management in hemodynamically unstable patients. (1C)

Glucose control
- Use a mechanical prophylactic device, such as compression stockings, for patients who are at very high risk for DVT. (1C)
- Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for DVT. (1C)
- In patients at very high risk LMWH should be used rather than UFH. (1C)

Renal replacement
- Use a mechanical prophylactic device, such as compression stockings, for patients who are at very high risk for DVT. (1C)
- Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for DVT. (1C)
- In patients at very high risk LMWH should be used rather than UFH. (1C)

Bicarbonate therapy
- Use a mechanical prophylactic device, such as compression stockings, for patients who are at very high risk for DVT. (1C)
- Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for DVT. (1C)
- In patients at very high risk LMWH should be used rather than UFH. (1C)

Deep vein thrombosis (DVT) prophylaxis
- Use a mechanical prophylactic device, such as compression stockings or an intermittent compression device, when heparin is contraindicated. (1A)
- Use either low-dose unfractionated heparin (UFH) or low-molecular weight heparin (LMWH), unless contraindicated. (1A)

Stress ulcer prophylaxis
- Provide stress ulcer prophylaxis using H₂ blocker or proton pump inhibitor. Benefits of prevention of upper GI bleed must be weighed against the potential for development of ventilator-acquired pneumonia. (1C)

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