Sepsis and Septic Shock: Update on Diagnosis and Management

JANE GUTTENDORF, DNP, CRNP, ACNP-BC, CCRN
ASSISTANT PROFESSOR
UNIVERSITY OF PITTSBURGH SCHOOL OF NURSING, DEPARTMENT OF ACUTE AND TERTIARY CARE
ADULT-GERONTOLOGY ACUTE CARE NURSE PRACTITIONER PROGRAM
ACUTE CARE NURSE PRACTITIONER
UPMC DEPARTMENT OF CRITICAL CARE MEDICINE
UPMC PRESBYTERIAN, SURGICAL ICU

Epidemiology of Critical Illness

- 5.7M patients admitted annually to ICUs in US
- 20% of acute care admissions are to ICU
- Up to 58% of ED admissions are to ICU

5 Primary Admitting Diagnoses for Adults:
1. Respiratory system diagnosis with ventilator support
2. Acute myocardial infarction
3. Intracranial hemorrhage or cerebral infarction
4. Percutaneous cardiovascular procedure with drug-eluting stent
5. Septicemia or severe sepsis without mechanical ventilation

http://www.sccm.org/Communications/Pages/CriticalCareStats.aspx (accessed 10/4/16)

Morbidity and Mortality

Overall mortality of patients admitted to adult ICUs is 10-29%.

Leading causes of death in the ICU:
- Multi-system organ failure
  - mortality rate up to 15-28% (when > one organ system fails)
- Cardiovascular failure
- Sepsis (2nd leading cause of death in non-coronary ICUs)
  - mortality rate up to 45%

http://www.sccm.org/Communications/Pages/CriticalCareStats.aspx (accessed 10/4/16)

Epidemiology

Comparison in Mortality, USA, by cause

- Acute Myocardial Infarction
- Septicemia
- Septic Shock

http://www.cdc.gov/vitalsigns/sepsis/
Measuring Organ Dysfunction:
**SOFA- Sequential Organ Failure Assessment Score**

Severity of illness scoring system used to predict mortality.

**Components:**
- PaO\textsubscript{2}\textasciitilde{FiO}_2
- Platelet count
- GCS
- Bilirubin
- Level of hypotension
- Creatinine

**Score 0 to 4 in each category**
- \(0\) = nil and \(4\) = high degree of organ dysfunction
- Scores range \(0\) to \(24\)

**Components:**

<table>
<thead>
<tr>
<th>PaO\textsubscript{2}/FiO\textsubscript{2} (mmHg)</th>
<th>SOFA score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 400</td>
<td>1</td>
</tr>
<tr>
<td>&lt; 300</td>
<td>2</td>
</tr>
<tr>
<td>&lt; 200 and mechanically ventilated</td>
<td>3</td>
</tr>
<tr>
<td>&lt; 100 and mechanically ventilated</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Glasgow coma scale</th>
<th>SOFA score</th>
</tr>
</thead>
<tbody>
<tr>
<td>13–14</td>
<td>1</td>
</tr>
<tr>
<td>10–12</td>
<td>2</td>
</tr>
<tr>
<td>6–9</td>
<td>3</td>
</tr>
<tr>
<td>&lt; 6</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bilirubin (mg/dl)</th>
<th>SOFA score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1.2 and (&lt; 20)</td>
<td>1</td>
</tr>
<tr>
<td>2.0–5.9 (≥20 and (&lt; 33))</td>
<td>2</td>
</tr>
<tr>
<td>6.0–11 (≥33 and (&lt; 100))</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 12 (≥100)</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MAP (&lt; 70) mmHg</th>
<th>SOFA score</th>
</tr>
</thead>
<tbody>
<tr>
<td>dops (&lt; 5) or doB (any dose)</td>
<td>1</td>
</tr>
<tr>
<td>dops (&gt; 5) OR epO (&lt; 0.1) OR nor (&lt; 0.1)</td>
<td>2</td>
</tr>
<tr>
<td>dops (&gt; 15) OR epO (&gt; 0.1) OR nor (&gt; 0.1)</td>
<td>3</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Creatinine (mg/dl)</th>
<th>SOFA score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 1.2 and (&lt; 20)</td>
<td>1</td>
</tr>
<tr>
<td>2.0–5.9 (≥20 and (&lt; 33))</td>
<td>2</td>
</tr>
<tr>
<td>3.5–4.9 (≥33 and (&lt; 50))</td>
<td>3</td>
</tr>
<tr>
<td>&gt; 5.0 (≥50)</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>PaO\textsubscript{2}/FiO\textsubscript{2} (mmHg)</th>
<th>SOFA score</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 400</td>
<td>1</td>
</tr>
<tr>
<td>&lt; 300</td>
<td>2</td>
</tr>
<tr>
<td>&lt; 200 and mechanically ventilated</td>
<td>3</td>
</tr>
<tr>
<td>&lt; 100 and mechanically ventilated</td>
<td>4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Glasgow coma scale</th>
<th>SOFA score</th>
</tr>
</thead>
<tbody>
<tr>
<td>13–14</td>
<td>1</td>
</tr>
<tr>
<td>10–12</td>
<td>2</td>
</tr>
<tr>
<td>6–9</td>
<td>3</td>
</tr>
<tr>
<td>&lt; 6</td>
<td>4</td>
</tr>
</tbody>
</table>

| SOFA- Sequential Organ Failure Assessment Score
Severity of illness scoring system used to predict mortality.

**Components:**
- PaO\textsubscript{2}/FiO\textsubscript{2}
- Platelet count
- GCS
- Bilirubin
- Level of hypotension
- Creatinine

**Score 0 to 4 in each category**
- \(0\) = nil and \(4\) = high degree of organ dysfunction
- Scores range \(0\) to \(24\)

**Interpretation:**

<table>
<thead>
<tr>
<th>Score</th>
<th>Predicted Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4</td>
<td>&lt; 10%</td>
</tr>
<tr>
<td>5-7</td>
<td>15-20%</td>
</tr>
<tr>
<td>8-10</td>
<td>30-50%</td>
</tr>
<tr>
<td>11-14</td>
<td>50-60%</td>
</tr>
<tr>
<td>15</td>
<td>&gt; 80%</td>
</tr>
<tr>
<td>16-24</td>
<td>&gt; 90%</td>
</tr>
</tbody>
</table>

Link to August 2016 CDC Vital Signs monthly report

http://www.cdc.gov/vitalsigns/sepsis/
Background on Sepsis Care

2001 - Early Goal-Directed Therapy (EGDT)
- ED based study
- Single center
- Focus early recognition of sepsis
- Early administration of antibiotics
- Placement of central line
- Goal directed resuscitation to targeted endpoints (CVP, MAP, ScvO2) for fluids, vasopressors, RBC transfusion, inotropes.
- Improved mortality

2004 - Surviving Sepsis Campaign
- Adopted EGDT protocol
- Defined sepsis care bundles to improve processes of care
- Focus early recognition
- Early administration of antibiotics
- Goal-directed fluid resuscitation to set the international standard of care for sepsis management
- Improved mortality

2004 - Surviving Sepsis Campaign
- Updated the 2004 guidelines
- Focused on education to improve processes of care for patients not in ICU settings
- Defined SIRS criteria, Sepsis, Severe Sepsis, Septic Shock and Sepsis-induced hypoperfusion
- Continued to advocate use of the sepsis resuscitation and management bundles:
  - 6hr: measuring initial lactate, BC prior to antbx, antbx within 3hrs ED admits or 1 hr non-ED admits, fluids 20ml/kg for hypotension, then early vasopressors to maintain MAP > 65. If persistent hypotension or lactate elevation (> 4 mmol/L), target CVP > 8 mmHg and ScvO2 > 70%.
  - 24 hr: Low-dose steroids for septic shock, drotrecogin alpha per hospital policy, glucose control < 150 mg/dL, inspiratory plateau pressures < 30cmH2O in mechanically ventilated patients.

2008 - Surviving Sepsis Campaign
- Updated the 2004 guidelines
- Major changes based on new evidence. Eliminated drotrecogin alpha, steroids, more liberal glucose targets.
- Importance of early recognition
- 3 hr bundle
- 6 hr bundle

2012 - Surviving Sepsis Campaign
- Updated the 2008 guidelines
- Major changes based on new evidence. Eliminated drotrecogin alpha, steroids, more liberal glucose targets.
- Importance of early recognition
- 3 hr bundle
- 6 hr bundle

3 Subsequent multi-center trials evaluating EGDT failed to replicate the mortality benefit demonstrated in the Rivers 2001 EGDT study (single center, 263 pts).
Reinforced importance of early recognition, early aggressive resuscitation and early antibiotics as mainstay of sepsis care.
- ProCESS Trial (US, 31 centers, 1341 pts) NEJM, 2014;370:1683-93.

17

Continuum of Sepsis

Surviving Sepsis Campaign 2012

SIRS
- Presence of two or more:
  - Temperature>38°C or <36°C
  - Heart rate >90/min
  - RR >20/m or PaCO2 <32 mmHg
  - WBC >12 or <4, or bands >10%

SEPSIS
- SIRS + Evidence of infection

SEVERE SEPSIS
- SEPSIS + Sepsis + organ dysfunction or tissue hypoperfusion
- Severe sepsis + hypotension despite fluid replacement
- Hypoperfusion = SBP < 90 or MAP <70

SEPTIC SHOCK
- Severe sepsis + hypoperfusion manifestations: lactic acidosis, oliguria, acute change in mental status

Third International Consensus Definitions of Sepsis and Septic Shock (Sepsis-3)

Problems with Prior Definitions
- Previous definitions highly sensitive, but not specific enough
- Many patients with non-infectious etiologies were included
  - pancreatitis, postoperative patients with stress response to surgery, etc.

New Definitions Proposed
- Joint task force of the Society of Critical Care Medicine (SCCM) and the European Society of Intensive Care Medicine (ESICM) developed new sepsis definitions and recommended screening

Summary of Changes
- SIRS criteria eliminated from the definition
  - (not required for sepsis definition, but still may be clinically useful)
- Term “Severe Sepsis” eliminated
  - (green mortality of sepsis near 11%, all sepsis is considered “Severe”)
- Eliminates the “continuum” concept
  - (patients can present with septic shock without preceding diagnosis of sepsis)
1. Infections still exist and can include signs of systemic inflammation, but do not meet the criteria for sepsis until signs of organ dysfunction are present.

2. Sepsis
   - Life-threatening organ dysfunction caused by a dysregulated host response to infection

3. Septic Shock
   - Subset of sepsis with profound circulatory, cellular and metabolic abnormalities which substantially increase mortality
   - Sepsis + Persistent hypotension requiring vasopressors to maintain MAP > 65 mmHg and lactate level > 2 mmol/L (> 18 mg/dL), despite adequate volume resuscitation

**qSOFA Score**

- Recommend use of quick SOFA score for screening patients with suspected infections.
  - Quick, easy, does not require invasive monitoring or blood testing

Quick SOFA (qSOFA) Criteria:
- RR > 22 breaths/min
- SBP (< 100 mmHg)
- Altered mental status (GCS < 15)

- Patients with 2 or more criteria are at significantly greater risk of death or prolonged ICU stay (3 or > days).

**Sepsis and Septic Shock**

Sepsis & septic shock are accompanied by signs and symptoms of acute organ dysfunction, hypotension and/or hypoperfusion including any of the following systems:

- Cardiovascular
- Respiratory
- Renal
- Hepatic
- Hematologic
- Central Nervous System

**Treatment Goals - Sepsis**

- Initial Resuscitation
  - Begin resuscitation IMMEDIATELY in patients with hypotension or elevated serum lactate > 4 mmol/L

- Early Aggressive management
  - Establish IV access
  - Laboratory studies (CBC w/ diff, lactate, BMP, appropriate cultures, imaging)
  - Volume resuscitation
    - Begin with 20-30ml/kg of crystalloid or colloid IV
  - Re-assess patient: heart rate, blood pressure, urine output, mental status
  - Collaborate with provider team
  - Central venous catheter access? TEE/ TEE

- Hypertension requiring vasopressors to maintain MAP > 65 mmHg
- Lactate > 2 mmol/L (18 mg/dL)

Hypoperfusion manifestations: lactic acidosis, oliguria, acute change in mental status
**Treatment Goals - Sepsis**

- **Early Aggressive Management**
  - Antibiotic therapy within 1 hour of recognizing severe sepsis & septic shock (based on likely source identified)
  - Antibiotics may be infused simultaneously
  - Begin with broad spectrum antibiotics until the causative organism & antibiotic susceptibility are identified
- **Continue with volume resuscitation until:**
  - CVP 8-12 mmHg
  - MAP > 65 mmHg
  - Urine output > 0.5ml/kg/hr
  - Lactate normalized

---

**Treatment Goals - Sepsis**

- **Early Treatment Goals**
  - If patient remains hypotensive (SBP < 90 or MAP < 65), consider vasopressors:
    - Norepinephrine
    - Place arterial line +/-
  - Re-assess patient: heart rate, blood pressure, urine output, mental status, peripheral perfusion
  - Additional treatment options for ongoing shock:
    - Inotropic therapy (poor evidence but can consider)
    - Steroid therapy
    - Blood transfusion (poor evidence)