Review of Current Sepsis Guidelines

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Objectives

• Define sepsis
• Compare and contrast scoring systems utilized in patient triage
• Review goals of therapy
• Utilize sepsis bundles to improve patient care
Definitions

- SIRS: Systemic inflammatory response syndrome
- SCCM: Society of Critical Care Medicine
- SOFA: Sequential organ failure assessment
- $\text{FiO}_2$: Fraction of inspired oxygen
- $\text{PaO}_2$: Partial pressure of oxygen
- GCS: Glasgow coma score
- MAP: Mean arterial pressure
- SCr: Serum creatinine
- qSOFA: Quick SOFA
- SBP: Systolic blood pressure
- EGDT: Early goal-directed therapy
- CVP: Central venous pressure
- $S_{\text{CVO}_2}$: Central venous oxygen saturation
WHAT IS SEPSIS?
Sepsis Overview

• Clinical syndrome caused by an exaggerated inflammatory response to infection
  – Fever
  – Hypotension
  – Leukocytosis
  – Coagulation cascade activation
  – Fibrinolytic activation

• Multiple organ failure can result
Localized infection

Excess cytokine release
- TNF α
- IL-1

SEPSIS
SEPSIS SCORING SYSTEMS: AN UPDATE
Out with the Old: SIRS

• Other medical conditions clouded the picture when using SIRS criteria
  – Tachycardia due to cardiac conditions
  – Respiratory rate due to asthma/COPD
  – Drug induced leukocytosis due to steroids

• Trauma, or any diagnosis that caused ischemia or inflammation also gave false positives
Out with the Old: SIRS

• 2016 SCCM sepsis panel unanimously voted it out of service
• Recommended replacing it with SOFA scoring system

JAMA 2016;315(8): 801-810
In with the New: SOFA

- Focused on organ dysfunction and morbidity
- Comprised of 6 variables, each representing an organ system
  - $\text{FiO}_2$, $\text{PaO}_2$, and mechanical ventilation $\rightarrow$ Lungs
  - Platelet count $\rightarrow$ Coagulation
  - Bilirubin $\rightarrow$ Liver
  - GCS $\rightarrow$ Neurological
  - MAP, and pressor use $\rightarrow$ Cardiovascular
  - SCr and urine output $\rightarrow$ Renal
In with the New: SOFA

<table>
<thead>
<tr>
<th>System</th>
<th>Score</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Respiration</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pao₂/Fio₂, mm Hg (kPa)</td>
<td></td>
<td></td>
<td>≥400 (53.3)</td>
<td>&lt;400 (53.3)</td>
<td>&lt;300 (40)</td>
<td>&lt;200 (26.7) with respiratory support</td>
</tr>
<tr>
<td><strong>Coagulation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Platelets, x10^3/μL</td>
<td>≥150</td>
<td></td>
<td>&lt;150</td>
<td>&lt;100</td>
<td>&lt;50</td>
<td>&lt;20</td>
</tr>
<tr>
<td><strong>Liver</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bilirubin, mg/dL (μmol/L)</td>
<td>&lt;1.2 (20)</td>
<td></td>
<td>1.2-1.9 (20-32)</td>
<td>2.0-5.9 (33-101)</td>
<td>6.0-11.9 (102-204)</td>
<td>&gt;12.0 (204)</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Dopamine &lt;5 or dobutamine (any dose)b</td>
<td>Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1b</td>
</tr>
<tr>
<td>MAP ≥70 mm Hg</td>
<td>MAP &lt;70 mm Hg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central nervous system</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glasgow Coma Scale score</td>
<td>15</td>
<td></td>
<td>13-14</td>
<td>10-12</td>
<td>6-9</td>
<td>&lt;6</td>
</tr>
<tr>
<td>Renal</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Creatinine, mg/dL (μmol/L)</td>
<td>&lt;1.2 (110)</td>
<td></td>
<td>1.2-1.9 (110-170)</td>
<td>2.0-3.4 (171-299)</td>
<td>3.5-4.9 (300-440)</td>
<td>&gt;5.0 (440)</td>
</tr>
<tr>
<td>Urine output, mL/d</td>
<td></td>
<td></td>
<td>&lt;500</td>
<td>&lt;200</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: Fio₂, fraction of inspired oxygen; MAP, mean arterial pressure; Pao₂, partial pressure of oxygen.

a Adapted from Vincent et al.27
b Catecholamine doses are given as μg/kg/min for at least 1 hour.

Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.
In with the New: SOFA

• Highest score for each variable collected every 24 hours

• Possible scores from 0-24

<table>
<thead>
<tr>
<th>Maximum SOFA Score</th>
<th>&lt; 7</th>
<th>7-9</th>
<th>10-12</th>
<th>13-14</th>
<th>15</th>
<th>&gt; 15</th>
</tr>
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<tbody>
<tr>
<td>Mortality</td>
<td>&lt; 10%</td>
<td>15-20%</td>
<td>40-50%</td>
<td>50-60%</td>
<td>&gt; 80%</td>
<td>&gt; 90%</td>
</tr>
</tbody>
</table>

Score Trend (first 48 hrs) | Mortality in Septic Shock
--- | ---
Increasing | > 50%
Unchanged | 27-35%
Decreasing | < 27 %


*JAMA.* 2001;286(14): 1754-8
In with the New: SOFA

• New guidelines define organ dysfunction based on SOFA score
  – SOFA ≥ 2 points from baseline
  – Corresponds to a mortality risk ≈ 10%

• Assume a baseline score of zero for patients with no preexisting organ dysfunction (acute or chronic)

_JAMA_ 2016;315(8): 801-810
qSOFA

• Useful bedside screen tool to predict sepsis in patients OUTSIDE the ICU
• Requires no lab values
• Patient given one point for each of 3 variables:
  1. Respiratory rate > 21/minutes
  2. Altered mental status
  3. SBP ≤ 100 mmHg
• Score > 1 associated with poor outcomes due to sepsis
GOALS OF THERAPY
Early Sepsis Goals

1. Stabilize respiration
2. Assess perfusion to peripheral tissues
3. Establish venous access
4. Restore perfusion
   - Crystalloid fluids
   - Vasopressor support
5. Administer appropriate antibiotics
6. Locate and address infection source
Early Sepsis Goals

• Fluid resuscitation in patients with hypoperfusion, defined as:
  – Hypotension persisting after initial fluid challenge
  – Blood lactate ≥ 4 mmol/L

• Broad-spectrum antibiotics within one hour of presentation

• Maintain MAP ≥ 65 mmHg
2016 Sepsis Guideline Update

• Removed EGDT for fluid resuscitation
  – No longer need to base fluid administration on CVP, $S_{\text{CVO2}}$ or other metrics
  – PROCESS, PROMISE, and ARISE trials found no mortality benefit to using EGDT

2016 Sepsis Guideline Update

• Give all hypotensive patients 30 mL/kg of crystalloid fluids
  – Assess for additional fluids based on dynamic measures
    • Passive leg raises
    • Fluid challenges against stroke volume measurements
    • Variations in systolic pressure, pulse pressure, or stroke volume
  – Administer further crystalloid fluids if needed
2016 Sepsis Guideline Update

• Norepinephrine as initial vasopressor of choice
  – May add vasopressin or epinephrine if needed
  – Avoid dopamine if possible
• Utilization of procalcitonin levels to shorten duration of antibiotic therapy
• Use IV hydrocortisone (200mg per day) only if hemodynamic stability not achieved through vasopressors and IV fluids
SEPSIS BUNDLES
What is a Sepsis Bundle?

- Central element in Surviving Sepsis Campaign
- Core tool in sepsis care improvement
- Simplify numerous steps in early sepsis patient care into more manageable “bundles”
What is a Sepsis Bundle?

- Broken into 3 and 6 hour steps
- Activated immediately upon identification of sepsis patient
- Adherence is associated with lower hospital mortality (20 vs 31%, p < 0.001)

*Intensive Care Med.* 2015; Sep;41(9): 1620-8
Three Hour Bundle

1. Measure lactate level
2. Obtain blood cultures prior to antibiotic administration
3. Administer broad spectrum antibiotics
4. Infuse 30 mL/kg of crystalloids if patient is hypotensive or elevated lactate level (≥ 4 mmol/L)
Six hour Bundle

5. Administer vasopressors to maintain MAP $\geq 65$ mmHg
6. Re-assess volume status and tissue perfusion
7. Re-measure lactate level if initial lactate elevated
Other Useful Tools

• Order sets incorporating sepsis bundles tailored to your facility
• Checklists and/or posters for staff
• EMR decision support
• Antimicrobial stewardship experts to narrow coverage after initial broad-spectrum empiric antibiotics started
References


Septic Case Study
Background

• Patient presented to the ER with complaint of left sided chest pain
• Described as intermittent and sharp (rated 7)
• Presents with nausea, vomiting and diarrhea
Background

- Complaining of diffuse abdominal pain (gets better when she drinks water)
- Complaining of shortness of breath (appears to be related to abdominal pain)
- On chronic opioids and ran out of her script about 48 hours ago
- Was receiving an antibiotic for kidney infection
Past Medical History

- CAD
- Coronary artery stent placement
- Carotid stenosis
- Pulmonary hypertension
- Chronic systolic congestive heart failure
- COPD
- Dyslipidemia
- Hypertension
- GI bleeding
Past Medical History

- Stage IV chronic kidney disease
- CABG
- Right Nephrectomy
- Type II diabetic
- DVT with IVC filter placed
- GERD
- Thrombophilia
ER Triage

• 1835 - Patient’s initial vital signs
  – BP: 133/102
  – P: 88
  – R: 21
  – O2: 98% on RA
  – Glasgow: 15
ER Triage

• 1859- Labs, EKG, Chest x-ray ordered

• 1913- Lab results
  • WBC-16.7*
  • Hgb- 14.4
  • Hct- 44.2
  • PLt- 474
  • PT- 22.4
  • INR- 2.2
  • Sodium- 138
  • Potassium- 4.8
  • Carbon Dioxide- 8.7* Venous

• Anion Gap- 30*
• BUN- 27*
• Creatinine- 1.93*
• Glucose- 119
• AST- 912*
• ALT- 551*
• P-BNP- 10903*
• ABG
  – pH 7.278*
  – CO2 16.3*
  – P02 152.0*
  – HCO3 7.4*
ER Triage

- Patient was given 4mg of morphine for her pain
- Patient was started on NS at 50cc/hr but was later discontinued.
- Patient was then transferred to CPCU
• Patient B/P increased to 210/69; HR 74; T: 96.4 Axillary
• Patient was given a dose of hydralazine 20mg IV once (2300 B/P 140/34)
• Patient was rating her pain 8/10
Transfer to CPCU

- 0030- FSBS was 31; 1 amp of D50 was given
- 0054- Lactate 9.7 and troponin 0.11 called to Doctor (Sepsis Alert Called)
- 0110- NS bolus (1 liter) at 1000cc/hr along with antibiotics
- NS to infuse at 150cc/hr
- Patient core temp 94.1 (F)
CPCU

- 0253- Patients core temperature is still 94.3, bear hugger started
- 0300- T= 95.0, HR = 98, B/P 104/45
- 0400- T= 96.8, HR = 104, B/P 113/51
- 0500- T= 97.2, HR = 100, B/P 119/55
- 0502- Labs called to doctor (no orders given)
- 0530- Update given to doctor (continue to monitor)

- 0400 Labs:
  - Carbon Dioxide 5.1*
  - BUN 28*
  - Creatinine 2.09*
  - AST 1355*
  - ALT 816*
  - WBC 19.6*
  - Lactate 9.6*
  - Procalcitonin > 200.00*

- 0500 Labs:
  - ABG
  - pH 7.181*
  - CO2 12.1*
  - P02 129.0
  - HCO3 6.0*
Transfer to ICU

• 0600- Patient transferred to ICU
• 0700- NS infusing at 150cc/hr
• Core temperature continued to be low throughout the morning of 96.1 but her vital signs were stable
• 0820- Abdomen US done (No significant findings)
• 1018- Lactate was 9.8
• 1100- NS with Bicarb started at 150cc/hr
ICU

- 1520- Blood pressure and temperature started decreasing
- 1520- T=94.6, HR 96, B/P 111/49
- 1645- NS bolus ordered and Levophed started at 5mcg/kg/min
- 1651- T= 94.6, HR 98, B/P 108/49
- 1746- Patient transferred to a accommodating facility

- 1616- Lab Values
  - Carbon Dioxide 6.4*
  - BUN 30*
  - Creatinine 2.38*
  - AST 2510*
  - ALT 1379*
  - Lactate 11.8*
SEPSIS CASE
Triage (Out-Lining Facility)

- 70 year old female was brought to the ER for tachycardia and shallow breathing and had audible secretions
- Patient was awake, cooperative, followed commands but was notably weak
- 12-lead showed patient was in SVT with rates in the 160’s
- Labs also showed she had an elevated troponin of 0.118
- Patient was given Adenosine 6mg IV and then 12mg IV and Zofran 4mg IV for nausea
- The patient converted to atrial fibrillation with RVR
- Patient was then transferred to HMC
Patients Past History

- Adenocarcinoma of the left lung with metastases to liver and brain
- Focal seizures secondary to brain metastases
- Chronic A-fib not on anticoagulation
- Hypertension
- COPD (continuous home O2 @ 4L/min)
- Type II diabetic, hyperlipidemia, hypothyroidism and depression
- MRSA positive
CPCU

- Patient was transferred to CPCU for A-Fib RVR under cardiology the patient was placed on a Cardizem gtt

- 1648- T 99.3, P 172, B/P 92/68, O2 91 on 4L/NC

- Between 1700 and 2020 HR of A-fib, RVR varied between 180’s to 150’s, B/P 110 to 95 systolic

- 1830 Cardiology consulted Hospitalist

- 2028- **Sepsis Alert** was called

- 2100 – Amiodarone gtt was started along with a bolus

- 2113 - Patient was then put on her own Bi-pap machine (which increased her O2 sat from 92% to 99%)

- 2130- NS bolus x 1 was ordered along with Doxycycline, Meropenem and Acyclovir

- 2114 Lab Values
  - Potassium 3.9
  - BUN 25
  - Creatinine 0.86
  - Phosphorous 2.0
  - Mg 1.2
  - L-Lactate 2.1*
  - Procalcitonin 20.45*
  - WBC 0.2*
  - Hgb 8.7
  - Platelets 44*

- **ABG**
  - pH 7.483
  - pCO2 33.2
  - P02 70.1
  - HCO3 24.6
ICU

2230 – T 102.9, HR 154, RR 24, B/P 91/45

2245- Patient was transferred to ICU for management of septic shock

2300 – T- 103.8, HR 140, RR 33, B/P 107/54

2315 - A cooling blanket was applied for temperature

2355 – T-102.2, HR 158, RR 31, B/P 81/55, 02 90% on 6 L/NC

0100- Patient’s respiratory status declined and was then intubated

Patient has had persistent diarrhea
ICU

• 0030 - Neo was started

• 0100 – T 104.9, HR 134, RR 23, B/P 60/34, O2 99 on 60%

• 0200– T 104.4, HR 136, RR 15, 68/54, O2 96%

• 0200- Left Art Line was placed

• 0230 - Triple lumen was placed, Neo was DC’d and Vasopressin was started at 2.4 units/hr, along with Levophed

• 0245 – HR 122, B/P 124/48, O2 97%
ICU

- 0350- Labs
  - Potassium 3.6
  - BUN 26
  - Creatinine 1.27
  - Troponin 0.20*
  - Lactate 4.0*
  - WBC 0.3*
  - Hgb 9.4
  - Plt Count 29*
- ABG
  - pH 7.177
  - CO2 60.7
  - P02 121
  - HCO3 21.6
ICU

• 0400 – ½ Normal Saline with 75mEq Bicarb was started at 100/hr

• 0400 – T 102.2, HR 116, RR 16, B/P 81/33

• 0430 – Albumin 5% bolus was given

• 0500 – T 102.4, HR 114, RR 24, B/P 100/42 02 97

• 0800 - Albumin 5% bolus was given

• 0930 - Lactate 7.1*
ICU

• 1030 to 1200 patients vitals averaged T-97.5, HR 92-96, RR 22-23, B/P 120’s to upper 110’s

• 1245- Lactate 9.1*

• 1316- Normal Saline bolus

• 1645- Labs
  • Lactate 7.2*
  • Potassium 3.6
  • BUN 27
  • Creatinine 1.58
  • Calcium 6.2*
  • WBC 1.0*
  • Platelet Count 12*
ICU

- 1730 - Normal Saline bolus

- 2113 – Lactate 7.2*

- 2130 – T- 100.4, HR 90, B/P 142/42

- 0000 – Lactate 6.8*

- 0400 - Labs
  - Potassium 3.6
  - BUN 29*
  - Creatinine 1.80*
  - Calcium 5.6*
  - Mg 1.6*
  - AST 760*
  - ALT 152*
  - Lactate 6.4*
ICU

- Patient continues on vasopressor support with Levophed 10mcg and Vasopressin at 2.4 mcg

- There was mottling bilateral lower extremities extending to anterior abdomen

- Cyanotic digits right upper extremity

- Decided to make patient comfort care

- Fact: Mortality from sepsis increases 8% for every hour that treatment is delayed.