Sepsis 3 & Early Identification

David Carlbom, MD
Medical Director, HMC Sepsis Program

Disclosures

- I have no relevant financial relationships with a commercial interest and will not discuss off-label use of a product or any investigational products.
- I do think systematic identification and rapid treatment of sepsis saves lives.

Objectives

- Be able to discuss the definition Sepsis 3
- Describe the importance of rapid identification
- Explain how the SePSIS early warning system can help identify sepsis patients
- Describe the challenges & opportunities of CMS Sepsis Core Measure
Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

Singer et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016

We have a definition for sepsis.

Criteria for the bedside?

Developing Bedside Criteria

- Use large electronic health record databases
- Identify those with suspected infection
- Study various existing organ dysfunc criteria
  - SOFA score
  - LODS score
  - SIRS criteria
SOFACL.png

**qSOFA**

Quick Sepsis - Related Organ Failure Assessment

qSOFA.org

**qSOFA as a clinical prompt**

- **Hypotension** SBP ≤ 100
- **AMS** GCS ≤ 13
- **Tachypnea** RR ≥ 22

- 2 of 3 criteria
- ~10% mortality

**Developing Bedside Criteria**

Seymour et al. JAMA 2016
Baseline “Risk” at the Bedside

- Baseline risk model using only age, demographics, race, co-morbidity
- Divide patients into deciles
- Compare validity within and across deciles

Baseline of baseline risk of in-hospital mortality

Decile of baseline risk of in-hospital mortality

Predictive validity of criteria: ICU

ICU encounters N = 7,932
Predictive validity of criteria: non-ICU encounters

N = 7,932

Decile of baseline risk of in-hospital mortality

Fold change, in-hospital mortality

SIRS ≥ 2 vs. SIRS < 2

SOFA ≥ 2 vs. SOFA < 2

LODS ≥ 2 vs. LODS < 2

qSOFA ≥ 2 vs. qSOFA < 2

Baseline risk (%)

Median

Test Performance

SOFA and LODS superior in the ICU

qSOFA similar to complex scores outside the ICU

qSOFA in external datasets

Seymour et al. JAMA 2016
SOFA

<table>
<thead>
<tr>
<th>Variable / Points</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>PaO2/FIO2 (mmHg)</td>
<td>&lt; 200</td>
<td>&lt; 300</td>
<td>&lt; 200</td>
<td>&lt; 100</td>
<td></td>
</tr>
<tr>
<td>Platelet Count (×10^9/L)</td>
<td>&lt; 100</td>
<td>&lt; 100</td>
<td>&lt; 50</td>
<td>&lt; 20</td>
<td></td>
</tr>
<tr>
<td>Glasgow Coma Scale</td>
<td>13 – 14</td>
<td>10 – 12</td>
<td>8 – 9</td>
<td>&lt; 8</td>
<td></td>
</tr>
<tr>
<td>Bilirubin (µmol/L / µmol/L)</td>
<td>1.2 – 1.9 / &gt;20 – 32</td>
<td>2 – 5.9 / &gt;20 – 101</td>
<td>8 – 11.9 / &gt;102 – 204</td>
<td>&gt;12 / &gt;204</td>
<td></td>
</tr>
<tr>
<td>MAP</td>
<td>No hypotension</td>
<td>MAP below 70</td>
<td>On vasoressors, dopamine &lt; 5 µg/kg/min or dobutamine (any dose)</td>
<td>Dopamine = 5 µg/kg/min or Forskolin x 1 µg/kg/min</td>
<td>Dopamine &gt; 10 µg/kg/min or Forskolin x 1 µg/kg/min</td>
</tr>
<tr>
<td>Creatinine (mg/dL / µmol/L)</td>
<td>&lt; 1.2 / &lt;106-168</td>
<td>1.2-1.9 / 106-168</td>
<td>2.0-3.6 / 177-321</td>
<td>3.5-6.9 / 306-433</td>
<td>&gt;6 / &gt;442</td>
</tr>
</tbody>
</table>

Serum lactate

Proportion of hospital mortality (%) vs. SOFA Score

Proportion of hospital mortality (%) vs. Serum lactate
Who is really, really, really sick?

Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.


Septic Shock

<table>
<thead>
<tr>
<th>Group</th>
<th>Hypotension p Fluids</th>
<th>Vasopress or</th>
<th>Lactate &gt;2mmol/L</th>
<th>Hospital Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>42.3%</td>
</tr>
<tr>
<td>2</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>30.1%</td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>28.7%</td>
</tr>
<tr>
<td>4</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>25.7%</td>
</tr>
<tr>
<td>5</td>
<td>No hypotension before</td>
<td>No</td>
<td>Yes</td>
<td>29.7%</td>
</tr>
<tr>
<td>6</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>18.7%</td>
</tr>
</tbody>
</table>


Septic Shock

- Sepsis with persisting hypotension requiring vasopressors to maintain MAP 65 mmHg
- Serum lactate level >2 mmol/L
- Despite adequate volume resuscitation

### 2003 vs 2016 Definitions

<table>
<thead>
<tr>
<th></th>
<th>2003</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>Suspected Infection + 2/4 SIRS Criteria</td>
<td>Delta SOFA ≥ 2 OR qSOFA ≥ 2</td>
</tr>
<tr>
<td>Severe Sepsis</td>
<td>Sepsis + Organ Dysfunction (variably defined)</td>
<td>N/A</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>Sepsis + Hypotension despite adequate fluid resus</td>
<td>Sepsis + Vasopressors needed MAP&gt;65 OR Lactate &gt; 2 despite adequate fluid resus</td>
</tr>
</tbody>
</table>

### What Next?

- SSC new guidelines targeted for Fall 2016 release
- CMS is not changing to new definition
- Don’t let “naming” your patient prevent good, prompt care of infection and organ dysfunction

### OK, How about 2am?

- Start with SIRS
- Treat Infection
  - Abx without delay
  - 30mL/kg volume
- qSOFA = 10% mort.
- SOFA
OK, How about 2am?

- Start with SIRS
- Treat Infection
  - Abx without delay
  - 30mL/kg volume
- qSOFA = 10% mort.
- SOFA

CMS Measure SEP-1

- Beginning 10/1/2015 discharges
- First year data gathering (refining criteria?)
- TBD: becomes part of Value Based Purchasing

CMS Definitions
CMS Definitions

- This patient has Severe Sepsis based on the following:
  - Sepsis Criteria present:
  - Tissue hypoperfusion persists in the hour after resuscitation fluids administered:
    - One of the following:
      - SBP < 90 mm Hg
      - MAP < 65 mm Hg
      - SBP decrease of > 40 mm Hg from baseline
      - Lactate ≥ 4 mmol/L

3 hour “bundle”

- Sepsis 3 hour bundle:
  - Measure lactate
  - Obtain blood cultures
  - Administer antibiotics
  - 30 mL/kg crystalloids

6 hour (shock) Bundle

- Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥65 mm Hg
- In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was ≥4, re-assess volume status and tissue perfusion and document findings
- Re-measure lactate if initial lactate elevated
Volume Re-assessment

Repeat Volume Status Assessment (within 6th of shock onset):
(If sepsis shock or initial lactate ≥5, choose one of following two methods)

- Focused exam
  - Document all of the following
    - Vital Signs
    - Cardiovascular exam
    - Capillary refill
    - Peripheral perfusion evaluation
    - Skin exam

- Other Methods of Fluid Reassessment
  - Document all of the following
    - Central venous pressure measurement
    - Central venous oxygen measurement
    - Blood lactate concentration decrease
  - Result
    - (if lactate ≥5, lactate ≥5 after lactate drop)
    - Positive Leg Raise or Fluid Challenge
      - PLE
      - Pulse Pressure x change
    - Fluid Challenge
      - % change + 25% target - 20% goal
    - Result
      - (pulse ox, change in 20 BP, pulse pressure variation in appendix, patient)

Post-Op Sepsis

- Incidence
- Mortality

<table>
<thead>
<tr>
<th>Condition</th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>2.3%</td>
<td>0.3%</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>1.6%</td>
<td>0.2%</td>
</tr>
<tr>
<td>PE</td>
<td>0.3%</td>
<td></td>
</tr>
<tr>
<td>AMI</td>
<td>0.2%</td>
<td></td>
</tr>
</tbody>
</table>
Screening at HMC

1. QSD Monitors SIRS Score
2. QSD Triggers Screening Order/Task
3. RN Completes Screening PowerForm
4a. RN Gets Immediate Feedback
4b. Page Sent to Care Team
5. QSD Triggers Follow-up Order/Task
6. RN Completes Follow-up PowerForm
7. Screening and Follow-up Documentation Adjust Trigger Criteria

Post-Op Sepsis

<table>
<thead>
<tr>
<th>Condition</th>
<th>Incidence</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>5.4%</td>
<td>9.1%</td>
</tr>
<tr>
<td>Sepsic Shock</td>
<td>33.7%</td>
<td>32.1%</td>
</tr>
<tr>
<td>PE</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMI</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

SePSIS Screening

- SIRS Sropped
- RN Administered
- RN reported infection
- Page sent to Care Team
- Follow-up

Screening resuming in 6h
Sepsis Classification

<table>
<thead>
<tr>
<th>Condition</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>43%</td>
</tr>
<tr>
<td>Severe Sepsis</td>
<td>15%</td>
</tr>
<tr>
<td>Septic Shock</td>
<td>3%</td>
</tr>
<tr>
<td>Septic Shock POA</td>
<td>3%</td>
</tr>
<tr>
<td>Septic Shock Dx in ICU</td>
<td>43%</td>
</tr>
</tbody>
</table>

Screening Performance

<table>
<thead>
<tr>
<th>Measure</th>
<th>Value</th>
<th>C.I.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>89%</td>
<td>85.7% - 91.3%</td>
</tr>
<tr>
<td>Specificity</td>
<td>51%</td>
<td>48.8% - 53.2%</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>31.6%</td>
<td>29.2% - 34.1%</td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>94.7%</td>
<td>93.2% - 95.9%</td>
</tr>
</tbody>
</table>

Antibiotic Timing & Survival

Kumar CCM 2006
Severe Sepsis

- Hospital Mortality
- Surviving Sepsis cohort
- 17,990 patients with severe sepsis
- Adjusted by severity, admit source, geography

Adjusted Mortality

Vasopressor Timing

- Septic Shock Patients
- Time to Norepinephrine
- 5.3% increase in mortality for every hour delay after 2 hours

Early Fluid

<table>
<thead>
<tr>
<th></th>
<th>Survivors</th>
<th>Non-survivors</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVF in First 3 hours</td>
<td>2085 mL</td>
<td>1600 mL</td>
<td>0.007</td>
</tr>
<tr>
<td>IVF in Hour 3.1 - 6</td>
<td>660 mL</td>
<td>880 mL</td>
<td>0.09</td>
</tr>
<tr>
<td>Total IVF in 6 hours</td>
<td>3150 mL</td>
<td>2875 mL</td>
<td>0.1</td>
</tr>
</tbody>
</table>

- higher proportion of fluid <3 hours associated with lower mortality

OR 0.34 (95% CI, 0.15 - 0.75)

Lee, Chest 2014

Bai, CritCare 2014
**RN-driven Care**

- RN notifies MD
- Draws lactate
- Draws cultures
- Initiates 500mL bolus

% Pts Meeting Goal

- Lactate: 48%
- Abx < 1hr: 56%
- Fluids 30mL/kg: 36%

Summary

- Seek out Sepsis & Infection
- Recognize SIRS is sensitive, may find earlier than qSOFA
- Design a standard method for rapid assessment
- Care team huddle, “Could this be sepsis?”