Sepsis in 2018: “ED, ICU, Surgical Perspectives”

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Disclosures

• Protocol writing committee and study planning committee member for VICTAS, Vitamin C, Thiamine, and Steroids in severe sepsis with cardiac or pulmonary dysfunction

• No other relevant sepsis-related disclosures
Critical Care

- Critical care is a concept not a location.
- It is a way of treating patients that begins in the pre-hospital setting with EMS care, continues in the ED, and is completed in the ICU.

Figure 2a: Incidence of Severe Sepsis by Method Over 6-year Period\textsuperscript{1}

\begin{itemize}
\item Angus
\item Wang
\item Dombrovskiy
\item Martin
\item Mean Weighted
\end{itemize}

\begin{itemize}
\item Number of Cases
\item Year
\end{itemize}

\textsuperscript{1} 95\% CI < 1\% of total for all data points and cannot be represented graphically.
Figure 2b: In-hospital Case Fatality of Severe Sepsis by Method

1 95% CI < 1%.
The Continuum of Sepsis

SIRS  Sepsis  Severe Sepsis  Septic Shock
The Continuum of Sepsis

SIRS  Sepsis  Severe Sepsis  Septic Shock
The Continuum of Sepsis

- SIRS
- Sepsis
- Severe Sepsis
- Septic Shock
The Continuum of Sepsis

SIRS  Sepsis  Severe Sepsis  Septic Shock
The Continuum of Sepsis

SIRS  Sepsis  Severe Sepsis  Septic Shock

Systemic Inflammatory Response Syndrome

SIRS criteria
- Temp $< 96.8^\circ \text{F}$ or $> 100.4^\circ \text{F}$
- HR $> 90$
- RR $> 20$ or PCO$_2 < 32$
- WBC $< 4$ or $> 12$ or bands $> 10\%$

Bone et al. Chest 1992
The Continuum of Sepsis

SIRS

Severe Sepsis

Septic Shock

Systemic Inflammatory Response to Infection

• Suspected or confirmed infection
• 2 or more SIRS criteria

Figure 1. The interrelationship between systemic inflammatory response syndrome (SIRS), sepsis, and infection.

Bone et al. Chest 1992
The Continuum of Sepsis

SIRS  Sepsis  Severe Sepsis  Septic Shock

Sepsis plus Organ Dysfunction
- Elevated Creatinine
- Elevated INR
- Altered Mental Status
- Elevated Lactate
- Hypotension that responds to fluid

Levy et al. Crit Care Med; 2003
The Continuum of Sepsis

SIRS  Sepsis  Severe Sepsis  Septic Shock

Cryptic Shock
• Normotensive
• Lactate ≥ 4

Severe Sepsis and Hypotension
• Hypotension that does NOT respond to fluid (30 cc/kg bolus)

Bone et al. Chest, 1992
Rivers et al. NEJM, 2001
New Sepsis Definition, 2016

- **Sepsis** is now defined as “life-threatening organ dysfunction caused by a dysregulated host response to infection”
- No more SIRS!
- Organ dysfunction: acute change in total SOFA score $\geq 2$ points due to the infection
- A SOFA score $\geq 2$ reflects an overall mortality risk of approximately 10%
The baseline Sequential (Sepsis-related) Organ Failure Assessment (SOFA) score should be assumed to be zero unless the patient is known to have preexisting (acute or chronic) organ dysfunction before the onset of infection. qSOFA indicates quick SOFA; MAP, mean arterial pressure.
Sensitivity vs. Specificity
Most common keywords related to septic patients’ symptom presentation

• Association between keywords and in-hospital mortality
  – abnormal/ suspected abnormal $T^\circ$ (64.1%)
  – pain (38.4%)
  – acute altered mental status (38.2%)
  – weakness of the legs (35.1%)
  – breathing difficulties (30.4%)
  – loss of energy (26.2%)
  – gastrointestinal symptoms (24.0%)

Wallgren et al. SJTREM, 2017
<table>
<thead>
<tr>
<th>Diagnosis (%)†</th>
<th></th>
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</thead>
<tbody>
<tr>
<td>Medical condition</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Pneumonia</td>
<td>39.5</td>
<td>38.5</td>
<td></td>
</tr>
<tr>
<td>Urosepsis</td>
<td>27.7</td>
<td>25.6</td>
<td></td>
</tr>
<tr>
<td>Peritonitis</td>
<td>4.2</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>21.9</td>
<td>23.1</td>
<td></td>
</tr>
<tr>
<td>Surgical condition</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraabdominal process</td>
<td>6.7</td>
<td>9.4</td>
<td></td>
</tr>
<tr>
<td>Source of sepsis — no. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>140 (31.9)</td>
<td>152 (34.1)</td>
<td>151 (33.1)</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>100 (22.8)</td>
<td>90 (20.2)</td>
<td>94 (20.6)</td>
</tr>
<tr>
<td>Intraabdominal infection</td>
<td>69 (15.7)</td>
<td>57 (12.8)</td>
<td>51 (11.2)</td>
</tr>
<tr>
<td>Infection of unknown source</td>
<td>57 (13.0)</td>
<td>47 (10.5)</td>
<td>66 (14.5)</td>
</tr>
<tr>
<td>Skin or soft-tissue infection</td>
<td>25 (5.7)</td>
<td>33 (7.4)</td>
<td>38 (8.3)</td>
</tr>
<tr>
<td>Catheter-related infection</td>
<td>11 (2.5)</td>
<td>16 (3.6)</td>
<td>11 (2.4)</td>
</tr>
<tr>
<td>Central nervous system infection</td>
<td>3 (0.7)</td>
<td>3 (0.7)</td>
<td>4 (0.9)</td>
</tr>
<tr>
<td>Endocarditis</td>
<td>1 (0.2)</td>
<td>3 (0.7)</td>
<td>3 (0.7)</td>
</tr>
<tr>
<td>Other</td>
<td>28 (6.4)</td>
<td>31 (7.0)</td>
<td>26 (5.7)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>18 (38)</td>
<td>19 (40)</td>
<td></td>
</tr>
<tr>
<td>Urosepsis</td>
<td>11 (23)</td>
<td>10 (21)</td>
<td></td>
</tr>
<tr>
<td>Primary bacteremia</td>
<td>7 (15)</td>
<td>7 (15)</td>
<td></td>
</tr>
<tr>
<td>GI/biliary</td>
<td>6 (13)</td>
<td>6 (13)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5 (11)</td>
<td>5 (11)</td>
<td></td>
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</tbody>
</table>
Early Recognition
87.9% SIRS-positive
12.1% SIRS-negative
tqSOFA

<table>
<thead>
<tr>
<th></th>
<th>Triage qSOFA&lt;2 (n=2337)</th>
<th>Triage qSOFA≥2 (n=508)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>56.2 ± 17.7</td>
<td>62.2 ± 17.8</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male</td>
<td>53% (1243)</td>
<td>51% (261)</td>
<td>ns</td>
</tr>
<tr>
<td>Time to Antibiotics (min) (n=2796)</td>
<td>197 ± 162</td>
<td>125 ± 114</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total IVF (mL) (n=2746)</td>
<td>2405 ± 1732</td>
<td>2750 ± 1857</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In hospital (n=2845)</td>
<td>11.7% (273)</td>
<td>26.4% (134)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>28 days (n=2459)</td>
<td>15.2% (308)</td>
<td>36.6% (159)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ICU Admission, (Y) (n=2845)</td>
<td>70.7% (1651)</td>
<td>78.2% (397)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Intubated (ED), (Y) (n=2836)</td>
<td>5.6% (130)</td>
<td>21.0% (106)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ALI (SF ratio&lt;452), (Y) (n=2845)</td>
<td>53.6% (1252)</td>
<td>77.8% (395)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Vasopressor(s), (Y) (n=2844)</td>
<td>5.6% (131)</td>
<td>14.4% (73)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

- tqSOFA≥2 for In-hospital mortality:
- Sens= 33%; Spec= 87%
- AUC, tqSOFA: 0.57 (95% CI: 0.55-0.59)
### qSOFA

<table>
<thead>
<tr>
<th></th>
<th>qSOFA&lt;2 (n=1478)</th>
<th>qSOFA≥2 (n=1362)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>54.8 ± 17.7</td>
<td>60.0 ± 17.6</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Male</td>
<td>54.3% (802)</td>
<td>51.4% (700)</td>
<td>ns</td>
</tr>
<tr>
<td>Time to Antibiotics (min) (n=2791)</td>
<td>204 ± 167</td>
<td>162 ± 141</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Total IVF (mL) (n=2763)</td>
<td>2172 ± 1524</td>
<td>2785 ± 1934</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Mortality</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>In hospital (n=2840)</td>
<td>8.5% (126)</td>
<td>20.6% (280)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>28 days (n=2457)</td>
<td>11.7% (150)</td>
<td>27.1% (316)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ICU Admission, (Y) (n=2840)</td>
<td>64.7% (956)</td>
<td>80.0% (1090)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Intubated (ED), (Y) (n=2830)</td>
<td>3.4% (50)</td>
<td>13.8% (187)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>ALI (SF ratio&lt;452), (Y) (n=2839)</td>
<td>45.2% (668)</td>
<td>71.5% (974)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Vasopressor(s), (Y) (n=2839)</td>
<td>2.5% (37)</td>
<td>12.3% (167)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

- qSOFA>=2 for In-hospital mortality:
- Sens= 70%; Spec= 56%
- AUC, qSOFA: 0.56 (95% CI: 0.55-0.57)
Organ Dysfunction?
ED Lactate in Severe Sepsis

Mikkelsen et al. CCM, 2009

Mortality (%) vs. Lactate (mmol/L)

- 0-1.9: 8.7%
- 2-3.9: 16.4%
- > 3.9: 31.8%

28-day Mortality

Normotensive
ED Lactate in Severe Sepsis

Mikkelsen et al. CCM, 2009
Time to Antibiotics

Inpatient Mortality (%) vs Antibiotic Timing

Gaieski et al. CCM, 2010
A 3-Hr Bundle

In-Hospital Mortality (%)

Time to Completion of 3-Hr Bundle (hr)

Crude
Risk adjusted

Seymour et al. NEJM, 2017
AIFR: Adequate Initial Fluid Resuscitation
CLFM: Conservative Late Fluid Management

Figure 3. Hospital mortality according to whether or not patients achieved AIFR, CLFM, both, or neither.