Sepsis Management and Hemodynamics

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- 2004: International group of experts, representing 11 organizations, published 46 guidelines to improve outcomes
- 2008: Revision of these guidelines
- Use of GRADE system to classify strength of recommendations -> large improvement guidelines
General Principle
Tissue Perfusion

Pressure
Flow
Adequacy

Hemodynamic Monitoring

Correct Measurement  Correct Interpretation  Application

How to Measure Intravascular Volume
• Effective intravascular volume
• Indirectly
  • CVP
  • PCWP
• Less indirectly
  • Ventricular Volume = Preload
  • Indices of Preload
    • LVEDP
    • LAP
Antibiotic Therapy

Intravenous antibiotic therapy must be started as early as possible and within the first hour of recognition of septic shock (1B) and severe sepsis without septic shock (1C).

Hospital Mortality by Time to Antibiotics

<table>
<thead>
<tr>
<th>Time to Antibiotics</th>
<th>OR</th>
<th>95% CI</th>
<th>p value</th>
<th>Probability of mortality</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 (ref)</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
<td>1.00</td>
</tr>
<tr>
<td>1</td>
<td>1.05</td>
<td>1.02</td>
<td>1.07</td>
<td>&lt; 0.001</td>
<td>19.0</td>
</tr>
<tr>
<td>2</td>
<td>1.09</td>
<td>1.04</td>
<td>1.15</td>
<td>&lt; 0.001</td>
<td>20.0</td>
</tr>
<tr>
<td>3</td>
<td>1.14</td>
<td>1.06</td>
<td>1.23</td>
<td>&lt; 0.001</td>
<td>20.8</td>
</tr>
<tr>
<td>4</td>
<td>1.19</td>
<td>1.09</td>
<td>1.32</td>
<td>&lt; 0.001</td>
<td>21.5</td>
</tr>
<tr>
<td>5</td>
<td>1.25</td>
<td>1.13</td>
<td>1.41</td>
<td>&lt; 0.001</td>
<td>22.3</td>
</tr>
<tr>
<td>6</td>
<td>1.30</td>
<td>1.13</td>
<td>1.51</td>
<td>&lt; 0.001</td>
<td>23.1</td>
</tr>
</tbody>
</table>

*Time to 48 h is based on 15,943 observations that are greater than or equal to zero.

Hospital mortality odds ratios referent group is < 6 hours for the time to 48 h and is adjusted by the number of baseline organ failures, infection type (community vs. nosocomial), and geographic region (Europe, North America, and South America).
Fluid therapy

- Crystalloids are recommended to be used in the initial fluid resuscitation of severe sepsis (Grade 1B).
- Albumin is recommended in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids (Grade 2C).

Fluid challenge

- Initial fluid challenge in sepsis-induced tissue hypoperfusion (hypotension or elevated lactate)
- A minimum of 30mL/kg of crystalloids (a portion of this may be albumin equivalent). (Grade 1B)

SSC Bundle: Sepsis 0500

To be completed within 3 hours of the presentation:

1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30mL/kg crystalloid for hypotension or lactate ≥4mmol/L

†“time of presentation” is defined as the time of triage in the Emergency Department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements severe sepsis or septic shock ascertained through chart review.
**Logistic Regression Model**

<table>
<thead>
<tr>
<th>Compliance indicator</th>
<th>Hospital mortality odds ratio</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Serum lactate within 6 hours</td>
<td>0.71</td>
<td>0.49–0.75</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2. Blood cultures before antibiotics</td>
<td>0.81</td>
<td>0.74–0.88</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>3. Blood culture positivity</td>
<td>0.83</td>
<td>0.72–0.95</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>4. Fluids and vasopressors</td>
<td>0.57</td>
<td>0.54–0.60</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>5. CVP ≥ 8 mm Hg within 6 hours</td>
<td>0.74</td>
<td>0.67–0.86</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>6. ScvO2 ≥ 70% within 6 hours</td>
<td>0.73</td>
<td>0.67–0.78</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>7. Reperfusion bundle</td>
<td>0.77</td>
<td>0.72–0.83</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>8. Low-dose norepinephrine policy</td>
<td>0.92</td>
<td>0.77–1.10</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>9. Overdosing norepinephrine policy</td>
<td>0.93</td>
<td>0.83–1.03</td>
<td>0.008</td>
</tr>
<tr>
<td>10. Glucose control maintained</td>
<td>0.70</td>
<td>0.62–0.78</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>11. IPP &gt; 30 cm H2O</td>
<td>0.78</td>
<td>0.71–0.86</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>12. Management bundle</td>
<td>0.72</td>
<td>0.65–0.79</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

**SSC Bundle: Sepsis 0500**

To be completed within 6 hours of time of presentation:

1. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation to maintain a mean arterial pressure (MAP) ≥ 65mmHg).

2. In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥ 4 mmol/L (36mg/dl):
   - Measure central venous pressure (CVP)*
   - Measure central venous oxygen saturation (ScvO2)*
   - Re-measure lactate*

* Targets for quantitative resuscitation included in the guidelines are CVP of ≥ 8 mm Hg, ScvO2 of ≥ 70% and lactate normalization.

**Vasopressors**

- Norepinephrine is recommended as the first choice vasopressor (Grade 1 B).
- Epinephrine is suggested (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain blood pressure (Grade 2B).
- Vasopressin .03 units/min can be added to norepinephrine with the intent of raising MAP to target or decreasing norepinephrine dosage. (UG)
Predefined subgroup analysis by type of shock


Meta-analysis – NE versus dopamine


Phenylephrine

Pure vasopressor and in general not recommended
Sepsis Induced Tissue Hypoperfusion

- Requirement for vasopressors after fluid challenge
  
  Or

- Lactate ≥ 4 mg/dL

Initial Resuscitation of Sepsis Induced Tissue Hypoperfusion

Recommend

Insertion central venous catheter
- Central venous pressure: 8–12 mm Hg
  - Higher with altered ventricular compliance or increased intrathoracic pressure (Grade 1C)

During Septic Shock

Diastole  Systole

Diastole  Systole

10 Days Post Shock
CO Measurement

- Indicator Dilution
- Doppler
- Arterial Pulse Wave

\[ \text{Area} = \text{diam} \times \pi / 4 \]
\[ SV = \text{Area} \times \text{VTI} \]

Effect on Stroke Volume

Pulse Contour
Effect on Cardiac Filling

- Continues measurement
- Less invasive than PAC
- Caveats
  - Descending Ao stroke volume
  - Probe not moving?

Esophageal Doppler

Initial Resuscitation of Sepsis Induced Tissue Hypoperfusion

Recommend

- Insertion central venous catheter
- ScvO2 saturation (SVC) ≥ 70%

Grade 1C
Lactate Clearance

In patients with elevated lactate levels as a marker of tissue hypoperfusion it is suggested targeting resuscitation to normalize lactate as rapidly as possible (grade 2C).

Where Do The Gains Live?

- Lead Time to Diagnosis
- Delivery of Proper Treatment
- Lead time to Diagnosis & Treatment

ProCESS¹

- Question current protocols (mortality did not reach statistical significance)
- Patients received at least two liters of saline prior to randomization
- 18% mortality in the usual care arm... (41% in Rivers paper² in 2001)
- Only addresses septic shock
- Two current randomized trials: The Australian Resuscitation in Sepsis Evaluation Randomised Controlled Trial (ARISE) and the Protocolised Management in Sepsis Trials (ProMISe)
- No serial lactate measurement ³ ⁴

². Rivers et al.. N Eng J Med 2001; 345:1368-1377
³. Jones et al.. JAMA 2010; 303:739-746
⁴. Jansen et al.. Am J Respir Crit Care 2010; 182:752-761
Thank You!!!

Baptist Health South Florida