Sepsis and Hemodynamic Support in 2017

September 15, 2017
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Objectives

- Review fluid resuscitation guidelines in septic shock
- Discuss volume assessment v. fluid responsiveness
- Evaluate pros and cons of various vasopressor options
- Discuss utilizing corticosteroids in septic shock
- Understand when to transfuse blood products in septic shock
Case

- 65 yo man with a history of HTN, CAD, ischemic cardiomyopathy (EF 45%) admitted with new onset AF with RVR, now s/p TEE and cardioversion
- Since admission, he has increasing cough and shortness of breath
- Temp 102.2; HR 118; BP 78/44; RR 24; O2 sat 89% on 6L NC
- WBC 16
- CXR with new RML consolidation

Case

- You order a vancomycin, zosyn due to concern for HCAP

**What should you do next?**

A. Give 2L IVF
B. Start norepinephrine 0.05mcg/kg/min
C. Insert right IJ CVC to assess CVP
D. Arrange for transfer to the MICU
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**Early Goal-Directed Therapy**

<table>
<thead>
<tr>
<th>PROCESS</th>
<th>PROMISE</th>
<th>ARISE</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Description</strong></td>
<td>31 EDs in the US; 2014</td>
<td>56 hospitals in England; 2015</td>
</tr>
<tr>
<td><strong>Study groups</strong></td>
<td>Three groups: EGDT (Rivers protocol) v. EGDT (no CVC, ionotropes, transfusions) v. usual care</td>
<td>Two groups: EGDT (6hrs) v. usual care</td>
</tr>
<tr>
<td><strong>Primary outcome</strong></td>
<td>No difference in 60-day mortality</td>
<td>No difference in 90-day mortality</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td>No difference in 90-day mortality, 1-year mortality or need for organ support</td>
<td>EGDT group had increased costs</td>
</tr>
</tbody>
</table>

### IVF Resuscitation

- Treatment and resuscitation should begin immediately
- Administer IV crystalloids at rate of at least 30cc/kg within the first 3 hours
- Additional fluids should be given based on reassessment of hemodynamic status
- Utilize dynamic (versus static) variables to predict fluid responsiveness
Fluid Therapy

- Crystalloids are the fluid of choice for initial resuscitation
- Balanced crystalloids preferred over normal saline
- Hydroxyethyl starches should not be used for resuscitation

<table>
<thead>
<tr>
<th>Assessment Tool</th>
<th>Marker</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>STATIC</td>
<td></td>
<td>Volume assessment</td>
</tr>
<tr>
<td>CVP (PAOP, LVEDP, IVC diameter)</td>
<td>Goal &gt; 8-12 to be considered &quot;volume replete&quot;</td>
<td></td>
</tr>
<tr>
<td>DYNAMIC</td>
<td></td>
<td>Fluid responsiveness</td>
</tr>
<tr>
<td>Pulse pressure variation (PPV)</td>
<td>&gt; 10-15% predictive of fluid responsiveness</td>
<td>No spontaneous respirations; Vt 8-12cc/kg; no arrhythmias</td>
</tr>
<tr>
<td>Passive leg raising test (PLR)</td>
<td>&gt; 10% in CO predictive of fluid responsiveness</td>
<td></td>
</tr>
<tr>
<td>Change in IVC diameter</td>
<td>12-18% variation predicts 10% increase in CO</td>
<td></td>
</tr>
<tr>
<td>Mini fluid challenge</td>
<td>&gt; 10% in subaortic velocity time interval (measured by echo) predictive of volume responsiveness</td>
<td></td>
</tr>
</tbody>
</table>
Is there such a thing as too much fluid?

### Table 4. 12-hr fluid balance: Survivors vs. nonsurvivors within CVP groups

<table>
<thead>
<tr>
<th>CVP Group</th>
<th>Survivors</th>
<th>Nonsurvivors</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Patients</td>
<td>3444 (1861-5681) mL</td>
<td>4429 (2537-6560) mL</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CVP &lt; 8 mm Hg</td>
<td>3015 (2056-4887) mL</td>
<td>2281 (802-5711) mL</td>
<td>NS</td>
</tr>
<tr>
<td>CVP 8-12 mm Hg</td>
<td>2727 (1227-5491) mL</td>
<td>3112 (1559-4869) mL</td>
<td>NS</td>
</tr>
<tr>
<td>CVP &gt; 12 mm Hg</td>
<td>3975 (2387-6614) mL</td>
<td>5237 (3140-7773) mL</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

CVP, central venous pressure; NS, nonsignificant. Volumes are expressed as median (25–75%).

Boyd JH et al, Crit Care Med, 2011

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**Case**

- You administer 2L of LR (~30cc/kg) but the patient remains hypotensive (MAP 52)
- Bedside U/S reveals global hypokinesis, depressed EF

**What should you do next?**

A. Give additional 2L IVF
B. Start norepinephrine 0.05mcg/kg/min and titrate for MAP > 65
C. Start dopamine 5mg and titrate for MAP > 65
D. Arrange for transfer to the MICU
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Vasopressors

De Backer (SOAPII), N Engl J Med, 2010
Vasopressors

![Forest Plot for Predefined Subgroup Analysis According to Type of Shock](image)

De Backer (SOAPII), N Engl J Med, 2010

**VASST trial**

- No significant difference in 28-day mortality or 90-day mortality
- Addition of vasopressin allowed decrease in norepinephrine while maintaining MAP

![Kaplan-Meier Survival Curves for Patients Who Underwent Randomization and Infusion](image)

Vasopressors

- “First choice” vasopressor is norepinephrine
- Vasopressin (up to 0.03 U/min) or epinephrine can be added to norepinephrine to increase the MAP or decrease norepinephrine dosages
- Dopamine should only be used in highly selected patients (weak recommendation, low quality of evidence)
- Dobutamine should be used in patient with persistent hypotension despite fluid loading and use of vasopressors (weak recommendation, low quality of evidence)

Case

- The patient is no longer responsive to IVF and his oxygenation continued to worsen requiring in intubation
- He is currently on norepinephrine 0.5mcg/kg/min and vasopressin 0.03
- The medical student asks you whether you should add stress dose steroids and you respond by saying...
Case

- “Should we give steroids?”
  A. Yes, but let’s complete an ACTH stim test first
  B. Sure, there isn’t a lot of evidence for them, but it (likely) won’t hurt
  C. Nope, there’s no evidence for steroids in septic shock
  D. Umm, let’s arrange transfer to the MICU
Corticosteroids in septic shock


Corticosteroids in septic shock

Annane, JAMA, 2002
What about steroids?

- “More trials needed”
- Emphasis should be placed ensuring adequate fluid resuscitation and vasopressor support
- If unable to achieve hemodynamic support with fluids and vasopressors, corticosteroids can be added
- Steroid dose is hydrocortisone 200mg IV (weak recommendation; low quality evidence)

And Blood Products?

[Graph showing time to death and probability of survival with different hemoglobin thresholds.]

And Blood Products?

**Table 2. Primary and Secondary Outcome Measures.**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Lower Hemoglobin Threshold</th>
<th>Higher Hemoglobin Threshold</th>
<th>Relative Risk (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary outcome: death by day 90 — no./total no. (%)</td>
<td>216/302 (43.0)</td>
<td>223/496 (45.0)</td>
<td>0.94 (0.78–1.09)</td>
<td>0.44</td>
</tr>
<tr>
<td><strong>Secondary outcomes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Use of life support — no./total no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At day 5</td>
<td>27/143 (17.6)</td>
<td>127/249 (51.4)</td>
<td>1.04 (0.95–1.14)</td>
<td>0.47</td>
</tr>
<tr>
<td>At day 14</td>
<td>140/360 (36.8)</td>
<td>133/367 (36.8)</td>
<td>1.00 (0.81–1.29)</td>
<td>0.09</td>
</tr>
<tr>
<td>At day 28</td>
<td>55/190 (28.9)</td>
<td>64/322 (19.9)</td>
<td>0.77 (0.54–1.09)</td>
<td>0.14</td>
</tr>
<tr>
<td>Ischemic event in the ICU — no./total no. (%)</td>
<td>35/488 (7.2)</td>
<td>39/489 (8.0)</td>
<td>0.90 (0.58–1.39)</td>
<td>0.64</td>
</tr>
<tr>
<td>Severe adverse reaction — no./total no. (%)</td>
<td>0/488</td>
<td>1/489 (0.2)</td>
<td>—</td>
<td>1.00</td>
</tr>
<tr>
<td>Alive without vasopressor or inotropic therapy — mean % of days</td>
<td>73</td>
<td>75</td>
<td>—</td>
<td>0.93</td>
</tr>
<tr>
<td>Alive without mechanical ventilation — mean % of days</td>
<td>65</td>
<td>67</td>
<td>—</td>
<td>0.49</td>
</tr>
<tr>
<td>Alive without renal replacement therapy — mean % of days</td>
<td>85</td>
<td>83</td>
<td>—</td>
<td>0.54</td>
</tr>
<tr>
<td>Alive and out of the hospital — mean % of days</td>
<td>30</td>
<td>31</td>
<td>—</td>
<td>0.89</td>
</tr>
</tbody>
</table>


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Transfusion Goals in Sepsis

- Transfuse PRBCs when hemoglobin is < 7 g/dL
- Transfuse platelets when < 10,000/mm³ in the absence of bleeding and < 20,000/mm³ if the patient has a risk of bleeding (weak recommendation, very low quality of evidence)

- **Do not transfuse FFP in the absence of bleeding or planned invasive procedure** (weak recommendation, very low quality of evidence)
Hemodynamic Support in Sepsis

- Identify sepsis
  - Start IV crystalloids at 30cc/kg within first 3 hrs
  - Use norepinephrine as “first-choice” vasopressor
  - Use vasopressin or epinephrine to raise MAP/decrease norepinephrine dosage
- Start antibiotics
- Ensure adequate source control
- Consider steroids

References

References