Cardiovascular Management of Septic Shock

R. Phillip Dellinger, MD
Professor of Medicine
Robert Wood Johnson Medical School/UMDNJ
Director, Critical Care Medicine and Med/Surg ICU
Cooper University Hospital
Camden, New Jersey
Septic Shock — A Melting Pot of Shock Etiologies

- Hypovolemic (loss of cardiac filling)
  - Capillary leak (absolute hypovolemia)
  - Venodilatation (relative hypovolemia)
- Cardiogenic
  - Decrease in contractility
- Obstructive
  - Rise in pulmonary vascular resistance
- Distributive (hypoperfusion despite normal/increased cardiac output)
MYOCARDIAL DYSFUNCTION IN SEPSIS

Left ventricular dysfunction
Right ventricular dysfunction

During Septic Shock

Diastole
Systole

10 Days Post Shock

Diastole
Systole
Septic Shock
Pre-Fluid Resuscitation

Increased Venous Capacitance

Increased Ventricular Compliance

Decreased Arteriolar Resistance

Sinus Tachycardia
Septic Shock Post-Fluid Resuscitation

Sinus Tachycardia

Capillary Bed

Capillary Leak
Question:
If ejection fraction (contractility) is decreased in sepsis, why is cardiac output usually increased?

Reasons:

(1) Tachycardia
(2) Decreased LV afterload
(3) Increase in LV compliance
Hemodynamic Profile in Severe Sepsis and Septic Shock

- Following volume resuscitation typically increased cardiac index with decreased systemic vascular resistance
Fluid Requirements in Sepsis

- Isotonic saline
- Hydroxyethyl starch
- 5% Albumin

What is the “Best” Fluid: Crystalloids vs Colloids?

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>#Pts</th>
<th>0.01</th>
<th>0.05</th>
<th>0.1</th>
<th>0.2</th>
<th>0.5</th>
<th>1</th>
<th>2</th>
<th>5</th>
<th>10</th>
<th>20</th>
<th>50</th>
<th>100</th>
<th>Relative</th>
<th>Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Love</td>
<td>1977</td>
<td>141</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.68</td>
<td>0.14-3.24</td>
</tr>
<tr>
<td>Lucas</td>
<td>1978</td>
<td>52</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.07</td>
<td>0.00-1.20</td>
</tr>
<tr>
<td>Butros</td>
<td>1979</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.22</td>
<td>0.12-4.12</td>
</tr>
<tr>
<td>Virgilio</td>
<td>1979</td>
<td>29</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.07</td>
<td>0.07-15.54</td>
</tr>
<tr>
<td>Moss</td>
<td>1981</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.43</td>
<td>0.11-55.69</td>
</tr>
<tr>
<td>Goodwin</td>
<td>1983</td>
<td>50</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.27</td>
<td>0.09-0.86</td>
</tr>
<tr>
<td>Modig</td>
<td>1983</td>
<td>23</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.06</td>
<td>0.02-50.43</td>
</tr>
<tr>
<td>Radvok</td>
<td>1983</td>
<td>26</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.23</td>
<td>0.71-2.11</td>
</tr>
<tr>
<td>Shires</td>
<td>1983</td>
<td>16</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.00</td>
<td>0.02-45.63</td>
</tr>
<tr>
<td>Metildi</td>
<td>1984</td>
<td>32</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.82</td>
<td>0.52-1.29</td>
</tr>
<tr>
<td>Sade</td>
<td>1985</td>
<td>33</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.33</td>
<td>0.04-90.08</td>
</tr>
<tr>
<td>Karanko</td>
<td>1987</td>
<td>32</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2.37</td>
<td>0.10-54.08</td>
</tr>
<tr>
<td>Davidson</td>
<td>1991</td>
<td>20</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.00</td>
<td>0.07-13.87</td>
</tr>
<tr>
<td>London</td>
<td>1992</td>
<td>90</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.22</td>
<td>0.01-3.93</td>
</tr>
<tr>
<td>Pockaj</td>
<td>1994</td>
<td>76</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.90</td>
<td>0.02-4.34</td>
</tr>
<tr>
<td>Overall</td>
<td></td>
<td>732</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.66</td>
<td>0.63-1.17</td>
</tr>
</tbody>
</table>

Monitoring for Excessive Increase in Pulmonary Capillary Pressure

- Physical exam
- Central venous pressure
- Pulmonary artery occlusion pressure
Hypotension Persists Despite Adequate Left Ventricular Preload

No PA Cath
- Combined inotrope/vasopressor

PA Cath
- Confirm adequate preload
- Inotrope targeted to maintain cardiac index 3.0
- Vasopressor targeted to maintain MAP 65 mm Hg

CVP catheter?
LeDoux D, Astiz ME, Carpati CM, Rackow EC

Effects of perfusion pressure on tissue perfusion in septic shock

Crit Care Med 2000; 28:2729-2732
<table>
<thead>
<tr>
<th></th>
<th>65 mm Hg</th>
<th>75 mm Hg</th>
<th>85 mm Hg</th>
<th>F/LT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>97 ± 4</td>
<td>101 ± 4</td>
<td>105 ± 5</td>
<td>.02/.02</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>65 ± 0.5</td>
<td>75 ± 0.4</td>
<td>86 ± 0.4</td>
<td>.0001/.0001</td>
</tr>
<tr>
<td>CI (L/min/m²)</td>
<td>4.7 ± 0.5</td>
<td>5.3 ± 0.6</td>
<td>5.5 ± 0.6</td>
<td>.07/.03</td>
</tr>
<tr>
<td>PAOP (mm Hg)</td>
<td>14 ± 1</td>
<td>15 ± 1</td>
<td>16 ± 1</td>
<td>.18/.16</td>
</tr>
<tr>
<td>LVSWI (g.m/m²)</td>
<td>45 ± 3</td>
<td>52 ± 5.5</td>
<td>63 ± 7</td>
<td>.01/.01</td>
</tr>
<tr>
<td>SVRI (dyne.sec/m².cm⁵)</td>
<td>998 ± 94</td>
<td>1065 ± 101</td>
<td>1216 ± 159</td>
<td>.09/.046</td>
</tr>
<tr>
<td>Norepinephrine (µg/min)</td>
<td>23 ± 22</td>
<td>31 ± 25</td>
<td>47 ± 39</td>
<td>.02/.016</td>
</tr>
<tr>
<td></td>
<td>65 mm Hg</td>
<td>75 mm Hg</td>
<td>85 mm Hg</td>
<td>F/LT</td>
</tr>
<tr>
<td>----------------------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>-------</td>
</tr>
<tr>
<td><strong>Urinary output (mL)</strong></td>
<td>49 ±18</td>
<td>56 ±21</td>
<td>43 ±13</td>
<td>.60/.71</td>
</tr>
<tr>
<td><strong>Capillary blood flow (mL/min/100 g)</strong></td>
<td>6.0 ± 1.6</td>
<td>5.8 ± 11</td>
<td>5.3 ± 0.9</td>
<td>.59/.55</td>
</tr>
<tr>
<td><strong>Red Cell Velocity (au)</strong></td>
<td>0.42 ± 0.06</td>
<td>0.44 ± 0.16</td>
<td>0.42 ± 0.06</td>
<td>.74/.97</td>
</tr>
<tr>
<td><strong>Pico₂ (mm Hg)</strong></td>
<td>41 ± 2</td>
<td>47 ± 2</td>
<td>46 ± 2</td>
<td>.11/.12</td>
</tr>
<tr>
<td><strong>Pa-Pico₂ (mm Hg)</strong></td>
<td>13 ± 3</td>
<td>17 ± 3</td>
<td>16 ± 3</td>
<td>.27/.40</td>
</tr>
</tbody>
</table>
Traditional Vasopressor Therapy of Septic Shock

- Dopamine
- Norepinephrine
- Phenylephrine
- Epinephrine
Norepinephrine vs Dopamine

Norepinephrine

- Greater effect on efferent as opposed to afferent glomerular arteriolar resistance
- Better preserved splanchnic perfusion?
- Venous bed constriction
  - less ADH release
  - less tachycardia
- No effect on hypothalamic – pituitary axis or intracranial pressure
- More suppression of tumor necrosis factor

NE had significantly lower hospital mortality (62% vs 82%) p<.001
Utility of Vasopressin in Septic Shock

Vasopressin and Shock

- Animal models of septic shock
- Septic versus cardiogenic shock
Effects of Dopamine, Norepinephrine, and Epinephrine on the Splanchnic Circulation in Septic Shock: Which is Best?

Circulating Vasopressin Levels in Septic Shock

Vasopressin and Septic Shock

- Human septic shock studies with low rates of infusion (.01-.04 units minute) decrease traditional vasopressor requirements.

So where do we stand with vasopressin therapy?

- Low dose vasopressin is very effective in decreasing or eliminating requirements of other vasopressors in septic shock

Concerns with routine use of vasopressin

- Effect on splanchnic circulation
- Effect on stroke volume and cardiac output
LMAB3001 - Kaplan-Meier Survival Curves
All Patients (Stages 1 & 2 combined)

KM Survival Estimate (%)

Day of Study

Placebo
n = 358

546C88
n = 436
C = Censored

Log-Rank: p=0.001
Discussed in SSC Guidelines Presentation

- Early goal directed resuscitation
- Steroid therapy
- Recombinant Activated Protein C
Reasonable Therapeutic Goals in Severe Sepsis with Hypoperfusion

- Mean arterial pressure of $60\text{–}65$ mm Hg
- Urine output of $\geq 0.5$ ml/kg/hr
- $\text{ScvO}_2 \geq 70\%$
- Reversal of lactic acidosis
- If cardiac output measured, $\geq 3.0$