Management of Sepsis and SIRS

Martin D. Black, MD
DISCLOSURES

• There has been no commercial support or sponsorship for this program.
• The planners and presenters have declared that no conflicts of interest exist.
• The program co-sponsors do not endorse any products in conjunction with any educational activity.
Boston College Connell School of Nursing Continuing Education Program is accredited as a provider of continuing nursing education by the American Nurses Association Massachusetts, an accredited approver by the American Nurses Credentialing Center’s Commission on Accreditation.
SESSION OBJECTIVES

• Differentiate between sepsis and SIRS.
• Describe the presentation and diagnosis of patients with sepsis and SIRS.
• Describe early and ongoing management strategies.
Diagnosis and Management of Sepsis and Septic Shock

Martin D. Black MD

Concord Pulmonary Medicine
Disclosures

• Financial: none
Outline

• Review of Shock

• Pharmacology of Vasopressor Drugs

• Sepsis
  – Definition
  – Epidemiology
  – Identification and risk stratification
  – Management
Case
“Jane”

• 70F “dysuria”
• 102F 22 91/50 115 98%ra
• Pyuria
• WBC 17k 12% bands
• CMP normal
• Lactate 5
Shock

- Shock ≡ Supply < demand

![Diagram of a train with.Hb] creditsaltHb creditsaltHb creditsaltHb creditsaltHb creditsaltHb creditsaltHb creditsaltHb creditsaltOxygen creditsaltTrack = vasculature creditsaltSpeed = CO
Lactic Acidosis

\[ \text{pyruvate} + \text{NADH} + \text{H}^+ \leftrightarrow \text{lactate} + \text{NAD}^+ \]

Anaerobic glycolysis

Cori cycle and oxidative phosphorylation (kidney, liver)

DDx: Global or regional hypoperfusion
     Mitochondrial injury
     Impaired hepatic clearance

Central Venous O2 Saturation

\[ \text{ScvO2} = 40\% \quad \text{ScvO2} = 70\% \]

\[ \text{SaO2} = 100\% \]

Extract 30% of DO2

Extract 60% of DO2
Ohms Law for Understanding Macrovascular Hemodynamics

\[ E = iR \]

\[ \Delta BP = CO \times SVR \]

\[ MAP = CO \times SVR + CVP \]
Vasopressor spectrum

\( \alpha_1 \)  \hspace{2cm} \beta_1 

phenylephrine  norepinephrine  dopamine  epinephrine  dobutamine  isoproterenol

vasopressin
Comparison of Dopamine and Norepinephrine in The Treatment of Shock (SOAP II trial)

- 1679 patients with any cause shock randomized to DA or NE with open-label pressors permitted for refractory hypotension

- Primary outcome: 28 day mortality

- Pre-specified subgroups of shock category

<table>
<thead>
<tr>
<th></th>
<th>DA</th>
<th>NE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septic</td>
<td>63.2 %</td>
<td>61.1%</td>
</tr>
<tr>
<td>Cardiogenic</td>
<td>15.7%</td>
<td>17.6%</td>
</tr>
<tr>
<td>Hypovolemic</td>
<td>16.1%</td>
<td>15.2%</td>
</tr>
<tr>
<td>% mechanical ventilator</td>
<td>71.7%</td>
<td>70.6%</td>
</tr>
</tbody>
</table>

Outcomes

- Arrhythmias 24.1% DA patients vs. 12.4% NE patients

Sepsis
Sepsis: Definitions

• **SIRS**:  
  – The systemic inflammatory response syndrome (SIRS) is clinically recognized by the presence of two or more of the following:
    • Temperature > 38°C or < 36°C
    • Heart rate > 90 bpm
    • Respiratory rate > 20 breaths/min or PaCO2 < 32 mmHg
    • WBC > 12,000, < 4000 or >10 percent bands
Sepsis: Definitions

• **Sepsis:**
  – Sepsis is the systemic response to infection.
    • “SIRS plus source (documented or suspected infection)”

• **Severe Sepsis:**
  – Sepsis is considered severe when it is associated with organ dysfunction, hypoperfusion, or hypotension.
Sepsis: Definitions

- **Septic Shock:**
  - Septic shock is sepsis with hypotension despite adequate fluid resuscitation combined with end-organ dysfunction.
  - Practically defined as SBP <90 despite adequate fluids
Inter-relationship of the Terms

Bone et al, Chest 1992; 101:1644
Sepsis: Epidemiology

• More than 750,000 cases of sepsis annually
  – Accounts for 215,000 deaths each year
    • This is more than AMI, lung cancer and other common causes of in-hospital death
  – Approximate cost: $17 billion per year

Approximately 200,000 patients including 70,000 Medicare patients have septic shock annually.
Epidemiology

Graph showing the trend of hospitalizations with septicemia or sepsis from 2000 to 2008. The rate per 10,000 population shows a significant linear trend from 2000 through 2008 for both categories. The source is CDC/NCHS, National Hospital Discharge Survey, 2000–2008.
Epidemiology

NOTES: Rates are significantly higher for males and females in each successive age group.
Identification

• History
• General variables (vital signs)
• Inflammatory (WBC, CRP, PCT)
• Hemodynamic (hypotension)
• Organ perfusion (lab screening)
• Tissue perfusion (lactate, mottled skin)

Lactic Acidosis in Sepsis

Management

• 2 Simultaneous tasks:
  – source control
  – hemodynamic normalization
Source Control

- Draw cultures prior to antibiotics
- Administer appropriate antibiotics <1 hour of development of severe sepsis/septic shock
- Attend to local drainage as soon as feasible (consider least invasive option)
- Antibiotics chosen to match clinical syndrome and consistent with local anti-biogram

Hemodynamic normalization

- Goal is restoration of normal cellular function

- Using macro-vascular parameters as guide (e.g. the train)

- Micro-vascular dysfunction is an area of ongoing research.
Micro-vascular Dysfunction in Sepsis

Disturbed microcirculation in sepsis

- Redistribution of organ blood flow
- DIC
- Cardiopulmonary pathology
- Disturbance of red and white cell rheology
- Viscosity alterations
- Vasoplegia
- Altered microvascular blood flow and vascular resistance
- Opening of AV shunts
- Edema formation
- Intravascular pooling
- Increased microvascular permeability
- Decreased red cell deformability
- Congestion and hemorrhage
- Endothelial activation

Micro-vascular Dysfunction in Sepsis

Stagnant flow

Normal

Stagnant and High Flow

Elbers PWG, Ince C. Critical Care 2006, 10:221
Surviving Sepsis Campaign Guideline
2013

A. Initial Resuscitation

1. Protocolized, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration \( \geq 4 \text{ mmol/L} \)). Goals during the first 6 hrs of resuscitation:
   
   a) Central venous pressure 8–12 mm Hg
   b) Mean arterial pressure (MAP) \( \geq 65 \text{ mm Hg} \)
   c) Urine output \( \geq 0.5 \text{ mL/kg/hr} \)
   d) Central venous (superior vena cava) or mixed venous oxygen saturation 70% or 65%, respectively (grade 1C).

2. In patients with elevated lactate levels targeting resuscitation to normalize lactate (grade 2C).
Early Goal-Directed Therapy

• Single Center
• N = 263
• Enrolled adults with at least 2 of 4 SIRS criteria and sbp <90 (despite IVF) or lactate >4mmol/L
• Randomized to EGDT protocol vs. Standard Care

Early Goal-Directed Therapy

Supplemental oxygen ± endotracheal intubation and mechanical ventilation

Central venous and arterial catheterization

Sedation, paralysis (if intubated), or both

CVP

- < 8 mm Hg: Crystalloid
- 8-12 mm Hg
  - MAP
    - < 65 mm Hg: Vasoactive agents
    - 65-90 mm Hg
      - ScvO₂
        - < 70%: Transfusion of red cells until hematocrit >= 30%
        - > 70%: Inotropic agents
    - > 90 mm Hg: No goals achieved

No goals achieved: Hospital admission

Yes: Hospital admission

Standard Therapy
CVP ≥ 8-12
MAP ≥ 65
UOP ≥ 0.5 mL/kg/hr
No explicit timeline
Hospital admission when bed available

## Early Goal-Directed Therapy: Results

<table>
<thead>
<tr>
<th></th>
<th>Standard</th>
<th>EGDT</th>
<th>RR (95%CI)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>In-hospital mortality</strong></td>
<td>46.5%</td>
<td>30.5%</td>
<td>0.58 (0.38-0.87)</td>
<td>0.009</td>
</tr>
<tr>
<td><strong>28 d mortality</strong></td>
<td>49.2%</td>
<td>33.3%</td>
<td>0.58 (0.39-0.87)</td>
<td>0.01</td>
</tr>
<tr>
<td><strong>60 d mortality</strong></td>
<td>56.9%</td>
<td>44.3%</td>
<td>0.67 (0.46-0.96)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Early Goal-Directed Therapy: Results

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hours after the Start of Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0–6</td>
</tr>
<tr>
<td>Total fluids (ml)</td>
<td></td>
</tr>
<tr>
<td>Standard therapy</td>
<td>3499±2438</td>
</tr>
<tr>
<td>EGDT</td>
<td>4981±2984</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Red-cell transfusion (%)</td>
<td></td>
</tr>
<tr>
<td>Standard therapy</td>
<td>18.5</td>
</tr>
<tr>
<td>EGDT</td>
<td>64.1</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Any vasopressor (%)†</td>
<td></td>
</tr>
<tr>
<td>Standard therapy</td>
<td>30.3</td>
</tr>
<tr>
<td>EGDT</td>
<td>27.4</td>
</tr>
<tr>
<td>P value</td>
<td>0.62</td>
</tr>
<tr>
<td>Inotropic agent (dobutamine) (%)</td>
<td></td>
</tr>
<tr>
<td>Standard therapy</td>
<td>0.8</td>
</tr>
<tr>
<td>EGDT</td>
<td>13.7</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mechanical ventilation (%)</td>
<td></td>
</tr>
<tr>
<td>Standard therapy</td>
<td>53.8</td>
</tr>
<tr>
<td>EGDT</td>
<td>53.0</td>
</tr>
<tr>
<td>P value</td>
<td>0.90</td>
</tr>
</tbody>
</table>

Steroids in Sepsis

Annane’s Prognostic study: JAMA 2000: “Three groups of prognoses were identified (using baseline cortisol and ACTH response):

Good: $\leq 34$ and $> 9$  (26% mortality at 28 days)

Intermediate: 34 and $\leq 9$ or $> 34$ and $> 9$ (67%) 

Poor: $> 34$ and $\leq 9$  (82%)

Annane D, et al; JAMA 2000;283:1083-1045
## Competing Trials

<table>
<thead>
<tr>
<th></th>
<th>Annane in JAMA 2002</th>
<th>CORTICUS – NEJM 2008</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Entry criteria</strong></td>
<td>Septic shock &lt; previous 3 hours</td>
<td>Septic shock &lt; previous 72 hours</td>
</tr>
<tr>
<td><strong>SAPS II</strong></td>
<td>57-60</td>
<td>48-49</td>
</tr>
<tr>
<td><strong>Initial lactate</strong></td>
<td>4.6</td>
<td>3.9-4.1</td>
</tr>
<tr>
<td><strong>Admission category</strong></td>
<td>~59% medical</td>
<td>~35% medical (rest elective/emergent surgery)</td>
</tr>
<tr>
<td><strong>Placebo mortality at 28 days</strong></td>
<td>53% (responders) 63% (non-responders)</td>
<td>28.8% (responders) 36.1% (non-responders)</td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>HC 50 mg q6 x 7 days FC 0.05 mg q24 x 7 days</td>
<td>50mg HC q6 x 5 days 50 mg HC q12 x 2 days 50 mg HC q24 x 3</td>
</tr>
<tr>
<td><strong># included at analysis</strong></td>
<td>299</td>
<td>499</td>
</tr>
<tr>
<td><strong>Mortality Difference by Responder status</strong></td>
<td>No difference for responders NR: OR 0.54 for death at 28 days</td>
<td>No difference for responders No difference for NR</td>
</tr>
<tr>
<td><strong>Time to shock reversal</strong></td>
<td>7 vs. 9 days (p 0.01) for all patients</td>
<td>3.3 vs. 5.8 days for all patients</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Steroid Summary

• Adjuvant hydrocortisone should be given to septic shock patients with vasopressor-dependence and high risk of death with hemodynamic instability despite resuscitation.

• ACTH should not be used to identify patients to receive steroids.
The Surviving Sepsis Campaign: Results of an international guideline-based performance improvement program targeting severe sepsis*

Severe Sepsis Bundles:

**Sepsis Resuscitation Bundle**
(To be accomplished as soon as possible and scored over first 6 hours):
1. Serum lactate measured.
2. Blood cultures obtained prior to antibiotic administration.
3. From the time of presentation, broad-spectrum antibiotics administered within 3 hours for ED admissions and 1 hour for non-ED ICU admissions.
4. In the event of hypotension and/or lactate > 4 mmol/L (36 mg/dl): a) Deliver an initial minimum of 20 ml/kg of crystalloid (or colloid equivalent). b) Apply vasopressors for hypotension not responding to initial fluid resuscitation to maintain mean arterial pressure (MAP) > 65 mm Hg.
5. In the event of persistent hypotension despite fluid resuscitation (septic shock) and/or lactate > 4 mmol/L (36 mg/dl):
   a) Achieve central venous pressure (CVP) of > 8 mm Hg.
   b) Achieve central venous oxygen saturation (ScvO2) of > 70%.*

**Sepsis Management Bundle**
(To be accomplished as soon as possible and scored over first 24 hours):
1. Low-dose steroids administered for septic shock in accordance with a standardized hospital policy.
2. Drotrecogin alfa (activated) administered in accordance with a standardized hospital policy.
3. Glucose control maintained > lower limit of normal, but < 150 mg/dl (8.3 mmol/L).
4. Inspiratory plateau pressures maintained < 30 cm H2O for mechanically ventilated patients.
   *Achieving a mixed venous oxygen saturation (SvO2) of 65% is an acceptable alternative.

© 2005 Surviving Sepsis Campaign and the Institute for Healthcare Improvement

Surviving Sepsis Campaign

• 15022 patients across 165 hospitals in North and South America and Europe

• Multifaceted intervention to improve compliance with the “Bundles”

Surviving Sepsis Campaign

Surviving Sepsis Campaign

Surviving Sepsis Campaign graph showing hospital mortality rate over different site quarters. The graph indicates a downward trend in hospital mortality from quarters 1 to 8. The asterisks (*) signify a p-value < 0.01 compared to site quarter 1.

Surviving Sepsis Campaign

After adjustment for baseline characteristics the following processes were associated with lower hospital mortality:

1) administration of broad-spectrum antibiotics
   (OR, 0.86; 95%, CI 0.79–0.93; p  .0001)

2) obtaining blood cultures before their initiation
   (OR, 0.76; 95% CI, 0.70–0.83; p  .0001)

3) maintaining blood glucose control
   (OR, 0.67; 95% CI, 0.62–0.71; p  .0001)
Lactate Clearance vs. ScvO2 for Early Sepsis

- N = 300 (3 hospitals)
- RCT of EGDT with SvO2 > 70% vs. EGDT with Lactate Clearance >10%
- Prospective non-inferiority design

- Treatments occurred in ER for 6 hours

Lactate Clearance RCT

<table>
<thead>
<tr>
<th>Intervention, h</th>
<th>Lactate Clearance Group (n = 150)</th>
<th>Scvo₂ Group (n = 150)</th>
<th>P Value&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crystalloid volume, mean (SD), L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-&lt;6</td>
<td>4.5 (2.36)</td>
<td>4.3 (2.21)</td>
<td>.55</td>
</tr>
<tr>
<td>6-72</td>
<td>12.4 (6.15)</td>
<td>11.8 (6.41)</td>
<td>.44</td>
</tr>
<tr>
<td>Vasopressor administration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-&lt;6</td>
<td>108 (72)</td>
<td>113 (75)</td>
<td>.60</td>
</tr>
<tr>
<td>6-72</td>
<td>100 (67)</td>
<td>108 (72)</td>
<td>.45</td>
</tr>
<tr>
<td>Dobutamine administration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-&lt;6</td>
<td>5 (3)</td>
<td>8 (5)</td>
<td>.57</td>
</tr>
<tr>
<td>6-72</td>
<td>10 (7)</td>
<td>13 (9)</td>
<td>.66</td>
</tr>
<tr>
<td>PRBC transfusion</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0-&lt;6</td>
<td>11 (7)</td>
<td>5 (3)</td>
<td>.20</td>
</tr>
<tr>
<td>6-72</td>
<td>35 (23)</td>
<td>31 (21)</td>
<td>.78</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variable</th>
<th>Lactate Clearance Group (n = 150)</th>
<th>Scvo₂ Group (n = 150)</th>
<th>Proportion Difference (95% Confidence Interval)</th>
<th>P Value&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality, No. (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intent to treat</td>
<td>25 (17)</td>
<td>34 (23)</td>
<td>6 (-3 to 15)</td>
<td></td>
</tr>
<tr>
<td>Per protocol</td>
<td>25 (17)</td>
<td>33 (22)</td>
<td>5 (-3 to 14)</td>
<td></td>
</tr>
<tr>
<td>Length of stay, mean (SD), d</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICU</td>
<td>5.9 (8.46)</td>
<td>5.6 (7.39)</td>
<td>.75</td>
<td></td>
</tr>
<tr>
<td>Hospital</td>
<td>11.4 (10.89)</td>
<td>12.1 (11.68)</td>
<td>.60</td>
<td></td>
</tr>
</tbody>
</table>

• RCT of N= 1341 across 31 Emergency Departments
• Entry criteria identical to other studies
• Primary outcome: 60 day mortality
• Compare 1 of 3 resuscitation strategies for 6 hours
  1. Early Goal Directed Therapy (i.e. Rivers)
  2. Protocol-based Standard Therapy
  3. Usual Care

Usual Care:
Clinician at the bedside having no mandated therapies

### PROCESS Trial

Care received from randomization to 6 hours.

<table>
<thead>
<tr>
<th></th>
<th>EGDT</th>
<th>PST</th>
<th>Usual Care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central Line Placed</td>
<td>93.6%</td>
<td>56.5%</td>
<td>57.9%</td>
</tr>
<tr>
<td>IV fluids (mL)</td>
<td>2805 +/- 1957</td>
<td>3285 +/- 1743</td>
<td>2279 +/- 1881</td>
</tr>
<tr>
<td>Vasopressor use</td>
<td>54.9%</td>
<td>52.2%</td>
<td>44.1%</td>
</tr>
<tr>
<td>Dobutamine use</td>
<td>8%</td>
<td>1.1%</td>
<td>0.9%</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>14.4%</td>
<td>8.3%</td>
<td>7.5%</td>
</tr>
</tbody>
</table>

• Secondary outcomes for resource utilization (LOS, etc.) were no different among groups

Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group*

- Prospective RCT
- N = 1600 (51 centers across Australia and New Zealand)
- Similar inclusion criteria as other studies
- EGDT vs Usual care (let to provider and no ScvO2 monitoring allowed)
- Primary outcome: 90 day mortality

NEJM 2014;371:1496-506
There was no significant difference in survival time, in-hospital mortality, duration of organ support, or length of hospital stay.

NEJM 2014;371:1496-506
Lessons from Protocolized Trials

• All trials screened patients at arrival
• IV fluid resuscitation was started early (even prior to randomization)
• Antibiotics were given early
• Evidence based supportive care was received
Antibiotic Stewardship

• Antimicrobial regimen should be reassessed daily for potential de-escalation.
• Use of low pro-calcitonin or similar biomarkers to assist discontinuation of empiric antibiotics in patient who initially appeared septic, but have no subsequent evidence of infection.
Pro-calcitonin

RCTs for use of PCT guided algorithm in ICU patients and in pneumonia have been shown to be non-inferior with regard to adverse events with fewer antibiotic days per patient.

JAMA. 2009;302(10):1059-1066
1381 patients admitted from ED with LRTI in Switzerland
Randomized to PCT-informed algorithm vs. standard care (5-10 days therapy by MD discretion)

Primary outcome: composite adverse events - death from any cause, ICU admission for any reason, disease-specific complications (i.e. persistence or development of pneumonia, lung abscess, empyema, and ARDS), and recurrence of LRTI in need of antibiotics with or without hospital readmission.

Secondary outcomes: antibiotic exposure, including duration of intravenous and oral antibiotic therapy, adverse effects from antibiotic treatment, and length of hospital stay.

Designed as non-inferiority trial
Control PCT after 6-24 hours

Initial antibiotics can be considered in case of:
- Respiratory or hemodynamic instability
- Life-threatening comorbidity
- Need for ICU admission
- PCT < 0.1 μg/l: CAP with PSI V or CURB65 >3, COPD with GOLD IV
- PCT < 0.25 μg/l: CAP with PSI ≥IV or CURB 65>2, COPD with GOLD > III
- Localised infection (abscess, empyema), L.pneumophila
- Compromised host defense (e.g. immuno-suppression other than corticosteroids)
- Concomitant infection in need of antibiotics

Consider the course of PCT

If antibiotics are initiated:
- Repeated measurement of PCT on days 3, 5, 7
- Stop antibiotics using the same cut offs above
- If initial PCT levels are >5-10 μg/l, then stop when 80-90% decrease of peak PCT
- If initial PCT remains high, consider treatment failure (e.g. resistant strain, empyema, ARDS)
- Outpatients: duration of antibiotics according to the last PCT result:
  - >0.25-0.5 μg/l: 3 days
  - >0.5 - 1.0 μg/l: 5 days
  - >1.0 μg/l: 7 days
Outcomes

- 15.4% in PCT group vs 18.9% in control had an adverse event outcome within 30 days of ED admission.
- The 95% CI for the risk difference (−7.6% to 0.4%) excludes an excess risk in the PCT group of 7.5%.

- CAP patients: Antibiotic exposure (median [IQR]) 7 [4-10] vs. 10 [8-12]) relative mean change −32.4% (−37.6 to −26.9)
- Adverse effect rate from antibiotics 23.5% vs. 33.1%; rate difference −9.6 (−15.4 to −3.8)

Figure 2. Antibiotic Exposure in Patients Receiving Antibiotic Therapy
Use of procalcitonin to reduce patients’ exposure to antibiotics in intensive care units (PRORATA trial): a multicentre randomised controlled trial

Prospective multi-center open-label RCT

621 patients admitted from ICU with suspected bacterial infection

Randomized to PCT-informed algorithm vs. standard care (therapy by MD discretion)

Primary outcome: 28-d mortality (non-inferiority), abx-free days (superiority)

<table>
<thead>
<tr>
<th></th>
<th>PCT</th>
<th>Standard</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>61 (+/-15.2) yrs</td>
<td>62.1 (+/- 15) yrs</td>
</tr>
<tr>
<td>% pneumonia</td>
<td>71</td>
<td>74</td>
</tr>
<tr>
<td>% mechanical ventilation</td>
<td>69</td>
<td>66</td>
</tr>
<tr>
<td>% septic shock</td>
<td>45</td>
<td>41</td>
</tr>
</tbody>
</table>

Guidelines for starting of antibiotics

- Concentration <0.25 μg/L
  - Antibiotics strongly discouraged

- Concentration ≥0.25 and <0.5 μg/L
  - Antibiotics discouraged

- Concentration ≥0.5 and <1 μg/L
  - Antibiotics encouraged

- Concentration ≥1 μg/L
  - Antibiotics strongly encouraged

If blood sample taken for calculation of procalcitonin concentration at early stage of episode, obtain a second procalcitonin concentration 6–12 h later

Guidelines for continuing or stopping of antibiotics

- Concentration <0.25 μg/L
  - Stopping of antibiotics strongly encouraged

- Decrease by ≥80% from peak concentration, or concentration ≥0.25 and <0.5 μg/L
  - Stopping of antibiotics encouraged

- Decrease by <80% from peak concentration, and concentration ≥0.5 μg/L
  - Continuing of antibiotics encouraged

- Increase of concentration compared with peak concentration and concentration ≥0.5 μg/L
  - Changing of antibiotics strongly encouraged

Outcomes

Summary:

• Severe sepsis and septic shock are common and constitute a high risk event for our patients.
• Timely recognition and therapy are key.
• Structured and coordinated care is important.
• Which (if any) protocol to use is unknown.
• Use antibiotics wisely.