R2R: Severe sepsis/septic shock

Surat Tongyoo
Critical care medicine
Siriraj Hospital
Diagnostic criteria

• ACCP/SCCM consensus conference 1991

• SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference 2001

• Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012
Diagnostic criteria for sepsis:
Infection, documented or suspected and some of the following:

**General variables**
- Fever (> 38.3°C) or Hypothermia (core temp < 36°C)
- Heart rate > 90/min or >2 SD over the normal value
- Tachypnea
- Altered mental status
- Significant edema or positive fluid balance
  - > 20 mL/kg over 24 hr
- Hyperglycemia
  - > 140 mg/dL in the absence of diabetes

**Inflammatory variables**
- Leukocytosis (WBC count > 12,000 μL)
- Leukopenia (WBC count < 4000 μL)
- Normal WBC count with immature forms > 10%
- Plasma C-reactive protein >2 SD above the normal value
- Plasma procalcitonin > 2 SD above the normal value

**Hemodynamic variables**
- Arterial hypotension (SBP < 90 mm Hg, MAP < 70 mm Hg, or an SBP decrease > 40 mm Hg in adults or < 2 SD below normal for age)

**Organ dysfunction variables**
- Arterial hypoxemia (Pao₂/Fio₂ < 300)
- Acute oliguria (urine output < 0.5 mL/kg/hr for at least 2 hrs despite adequate fluid resuscitation)
- Creatinine increase > 0.5 mg/dL or 44.2 μmol/L
- Coagulation abnormalities (INR > 1.5 or aPTT > 60 s)
- Ileus (absent bowel sounds)
- Thrombocytopenia (< 100,000 /μL)
- Hyperbilirubinemia (plasma total bilirubin > 4 mg/dL or 70 μmol/L)

**Tissue perfusion variables**
- Hyperlactatemia (> 1 mmol/L)
- Decreased capillary refill or mottling

Diagnostic criteria

- **SIRS**: 2 or more of the following conditions
  - Temperature > 38.5 or < 35.0 °C
  - Heart rate > 90 bpm
  - Respiratory rate > 20 /min or PaCO₂ < 32 mmHg
  - WBC > 12,000 /ml, < 4,000 /ml or Immature > 10%

- **Sepsis**: SIRS + Documented infection
  - Culture or Gram stain of blood, sputum, urine, or normally sterile body fluid positive for pathogenic microorganism
  - Focus of infection identified by visual inspection, *eg*, ruptured bowel with free air or bowel contents found in abdomen at surgery, wound with purulent discharge
Diagnostic criteria

- **Severe sepsis** : Sepsis + 1 organ dysfunction
  - **Kidney** - urinary output of < 0.5 mL/kg for at least 1 h or 
    - renal replacement therapy or 
    - creatinine increase > 0.5 mg/dL
  - **Heart** - cardiac dysfunction (*echocardiography*)
  - **Lung** - acute lung injury/ARDS (*PaO₂/FiO₂ < 300*)
  - **CNS** - abrupt change in mental status or abnormal EEG findings
  - **GI** - bowel ileus, absent bowel sound, hyperbilirubin (total > 4 mg/dL)
  - **Skin** - areas of mottled skin; capillary refilling of ≥ 3 second
  - **Peripheral tissue** - lactate > 2 mmol/L
  - **Blood** - platelet count of < 100,000 cells/mL or 
    - disseminated intravascular coagulation, 
    - coagulopathy (INR > 1.5, aPTT > 60 sec)
Diagnostic criteria

• **Septic shock**
  - Severe sepsis + one of the following conditions
    - Systemic mean BP of < (60) 70 mm Hg (< 80 mm Hg if previous hypertension) after 20–30 mL/kg starch or 40–60 mL/kg serum saline solution or PCWP between 12 and 20 mm Hg
    - Need for dopamine of > 5 mcg/kg/min, or norepinephrine or epinephrine of > 0.25 mcg/kg/min to maintain mean BP at > (60) 70 mm Hg (80 mm Hg if previous hypertension)
Correlation of mortality rate and severity of disease

- Septic shock (n = 1,134)
- Severe sepsis (n = 827)
- Sepsis (n = 1,063)
- Infection, no SIR (n = 584)

AJRCCM 2003; 168: 77-84.
Incidence of severe sepsis: Age dependence

Crit Care Med 2001; 29:1303–1310
• 9 million Thai people age > 60 years old
  – Estimated 100,000 septic shock patients
• In the next decade, 18 million Thai people age > 60 years old
  – Estimated >200,000 septic shock patients
Clinical significance

• **High incidence**
  – 2-5% of hospitalization patient
  – Incidence increasing in elderly

• **High mortality**
  – 30-60%

• **High cost**
  – USA = 663,000 Thai baht/case
  – Siriraj = 240,000 Thai baht/case
**Inclusion criteria**
- 2-4 criteria for SIRS
- Systolic BP <90 mmHg after 20-30 ml/Kg crystalloid in 30 min
- Blood lactate ≥ 4 mmol/L

**Result**
- 28d mortality 49.2 vs 33.3%, OR 0.58(0.39-0.87), P=0.01
- 60d mortality 56.9 vs 44.3%, OR 0.67(0.46-0.96), P=0.03
- Sudden cardiac death
- 21 vs 10.3%, P=0.02
Siriraj septic shock guideline

- เริ่มปี พ.ศ. 2545
- ใช้เฉพาะในภาควิชาอายูรศาสตร์
- โดยเฉพาะใน ICU
- คาดว่าจะลดอัตราการเสียชีวิตของผู้ป่วย septic shock
- จากร้อยละ เป็นร้อยละ
Problems

• Incidence of severe sepsis and septic shock in Siriraj hospital
• Outcome of previously use treatment strategy
• What is/are the prognostic determining factors?
• How can we improve our patients’ outcome?
Clinical significance

Epidemiology of Sepsis in Siriraj Hospital 2007

Nasikarn Angkasekwain MD*,
Pinyo Rattanarumpawan MD*, Visanu Thamlikitkul MD*

*Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Sepsis remains a major health burden, and there is limited epidemiological report of sepsis in Thailand.

Objective: To determine the epidemiology, treatments, clinical courses and outcomes of sepsis patients.

Material and Method: All sepsis patients in medical wards at Siriraj Hospital were recruited from February 1 to July 31, 2007. The information from patients’ medical records were retrieved and analyzed.

Results: From 3,451 patients, 201 (5.8%) were diagnosed as sepsis, and 38.8% of these developed septic shock. Among sepsis patients, 62.2% were community acquired, 40.8% had bacteremia, and gram negative bacteria were the common pathogen (51.7%). Appropriate antibiotics were given within 6 hours in 39%. Goal-directed therapy was achieved in only 11.5%. The mortality among sepsis and septic shock patients was 34.3% and 52.6%, respectively (p = 0.008). Risk factors for hospital mortality included higher maximum SOFA score, hospital-acquired infection, central nervous system dysfunction and receiving antibiotics after 6 hours of onset of sepsis.

Conclusion: Sepsis is still common and has contributed to high mortality. Goal directed therapy and appropriate antibiotics given within 6 hours might improve the outcome.

Keywords: Sepsis, Shock, Septic

Full text, e-Journal: http://www.maj.or.th/journal

- During 6 months period
  - Feb – July 2050
- 3451 medical patients
  - 201 were diagnosed sepsis
  - 182 were severe sepsis
  - 5.3 : 100 admission
  - 78 developed septic shock
- Mortality rate
  - Severe sepsis = 34.3%
  - Septic shock = 52.6%
Impact of Septic Shock Hemodynamic Resuscitation Guidelines on Rapid Early Volume Replacement and Reduced M

Chairat Permpikul MD*, Surat Tongyoo MD*, Ranista Ratanaat MD*, Warakam Wilachone MD*, Aekarin Poompichet MD*

* Division of Critical Care, Department of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

**Background:** Septic shock is one of the most serious conditions associated with high mortality. We recently developed a modified septic shock management guideline focusing on rapid restoration of hemodynamics by using clinical endpoint. Our aim was to analyze patients' outcomes following the guideline implementation.

**Material and Method:** A retrospective review of hemodynamic data sheet and clinical outcomes of patients admitted to medical ICU and medical Wards and during June 2004 and February 2006.

**Results:** One hundred and four patients' records were retrieved. The patients' mean age was 62.5 ± 18.6 year. Their mean APACHE II score were 24.9 ± 6.7 and the overall mortality was 59%. Sixty eight patients (65.4%) underwent guideline directed therapy (guideline group). The guideline group received higher volume resuscitation from the first hour of resuscitation (1,016.3 ± 675.0 ml vs. 521.4 ± 359.2 ml, p < 0.001) to the forty eighth hour (10,096.9 ± 3,256.1 ml vs. 8,067.3 ± 2,591.9 ml, p = 0.006). More of them achieved the therapeutic goal within 6 hours (60.8% vs 44.4%, p < 0.001) and their hospital mortality was lower (41.2% vs 69.4%, p = 0.008). When analyzing differences between those who survived and those who died, more of the surviving patients underwent guideline directed treatment (79.5% vs 55%, p = 0.012). They received higher volume replacement from the first hour to the end of the twelfth hour (first hour 1,098.0 ± 723.0 vs 660.9 ± 478.9 ml, p < 0.001; the end of the twelfth hour 3,746.6 ± 1,799 vs. 3,014.1 ± 1,579.9 ml, p = 0.038) and more of them achieved the therapeutic goal within 6 hours (95.5% vs 55%, p < 0.001). Multivariate analysis of factors associated with mortality disclosed APACHE II score, volume resuscitation more than 800 ml in the first hour and achievement of the therapeutic goal within 6 hours.

**Conclusion:** Implementation of our modified septic shock guideline is associated with rapid initial volume replacement, prompt achievement of therapeutic goal and improved outcomes. Volume resuscitation greater than 800 ml in the first hour is associated with better survival.

**Keyword:** Septic shock, Hemodynamic guideline, Fluid therapy

Full text, e-Journal: http://www.mmat.or.th/journal

---

The first study

**Overall mortality 59%**

**Guideline oriented 65.4%**

**Better outcome in guideline used group**

- Achieve goal in 6 hrs
  - 86.8 vs 44.4%, P<0.001
- Hospital mortality
  - 41.2 vs 69.4%, P=0.008

**Factors predicted outcome**

- Lower APACHE II score
- 1st hr volume > 800mL
- Achieve goal in 6 hrs
Correlation of 1\textsuperscript{st}hr volume and survival rate

\begin{align*}
\text{Volume 1\textsuperscript{st}hr} &
\begin{array}{l}
<400ml \\
400-799ml \\
800-1199ml \\
>1200ml \\
\end{array} \\
\text{Percent} &
\begin{array}{l}
0\% \\
10\% \\
20\% \\
30\% \\
40\% \\
50\% \\
60\% \\
70\% \\
\end{array} \\
\text{Survival rate} &
\end{align*}

P=0.012
Survival of septic shock: Impact of rapid volume resuscitation

Odds ratio 0.28
[0.10-0.69]
P=0.006
Can we further improve outcome

- Promote fluid resuscitation in the 1st hour

- Problems
  - Complication of fluid overload

- Central venous pressure (CVP)
  - Low CVP insertion rate, only 15%
  - Unable to follow ScvO2
• Include 300 severe sepsis/septic shock patients

• Intervention
  – EGDT: ScvO₂ goal
    • ScvO₂ > 70
  – EGDT: Lactate clearance
    • Lactate decrease > 10% in 2-6hrs
Lactate and shock management

- Blood lactate level
  - Increased serum lactate
    - Type A lactic acidosis
      - Inadequate tissue $O_2$
      - Shock related
    - Type B lactic acidosis
      - Metformin, methanol, ethylene glycol, nucleoside reverse transcriptase inhibitors
Lactate and shock management

• The correlation of lactate and ScvO$_2$ level

• Is there any difference of lactate level in capillary, venous and arterial blood specimen?

• How often we should send the blood lactate?
Correlation of Arterial, Central Venous and Capillary Lactate Levels in Septic Shock Patients

Pattharawin Pattharanitima MD*, Surat Tongyoo MD**,
Ranitha Rataniarat MD**, Warakam Wilachone MD**,
Aekarin Poompichet MD**, Chaiwat Permpikul MD**

*Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand
**Division of Critical Care Medicine, Department of Medicine, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

Background: Blood lactate level increases in response to tissue hypoxia and this level is currently used to monitor shock management. To obtain the arterial lactate value in clinical practice is a time consuming process. Our previous study demonstrated good correlation between the capillary lactate determined by a portable lactate analyzer and the standard arterial lactate in critically ill patients. This study aimed to examine the uses of this capillary lactate in septic shock.

Material and Method: A prospective comparison of arterial, venous and capillary lactate level from septic shock patients admitted in the general wards and the Medical ICU, Department of Medicine, Siriraj hospital was performed during October 2009 to February 2010.

Results: Thirty patients were included in the study. The mean age was 66 (24-86) years and 16 (53%) were female. The correlation between arterial and central venous was 0.992 and the correlation between arterial and capillary lactate level was 0.945 (p = 0.01 in both comparisons). In addition, there was certain agreement between the arterial and the capillary lactate especially when arterial lactate was below 10 mmol/L.

Conclusion: The capillary lactate level determined by the portable lactate analyzer (Accutrend® Plus) correlated well with arterial lactate level. This method, when used cautiously, may be used to monitor septic shock treatment as an alternative to the standard arterial lactate determination.

Keywords: Arterial lactate, Central venous lactate, Capillary lactate, Septic shock

J Med Assoc Thai 2011; 94 (Suppl. 1): S175-S180
Full text, e-Journal: http://www.maj.or.th/journal

The 2nd study

Good correlation of serum lactate from capillary, venous and arterial blood

- A lactate = V lactate
- C lactate = A lactate + 1
The 3rd study

Low ScvO₂ associated with high serum lactate

However, too high ScvO₂ > 85% in septic shock patient associated with high serum lactate and very poor outcome
Goal of shock management
Can we further improve outcome

- Promote fluid resuscitation in the 1st hour
- We can use serum lactate clearance as an indicator for adequate tissue perfusion
- To use lactate clearance, we have to send blood for lactate level at the initial resuscitation time and following serum lactate once the patient’s BP > 60-65 mmHg
Can we further improve patient’s outcome?

- What is the most appropriate BP goal?
- Are current hemodynamic goals good enough?
- Should we admit septic shock patient directly into ICU for better outcome?
The 4th study

- To evaluate the impact of hemodynamic goals achievement rate and the patients’ outcome
- Prospective study
- Included 175 severe sepsis and septic shock patients

**Background:** Severe sepsis and septic shock are associated with high mortality. “Early goal-directed therapy” (EGDT) has been shown to improve survival. The authors report here the goal achievements in the protocol and their association with patients’ outcomes.

**Material and Method:** A prospective cohort study of patients with severe sepsis and septic shock who were admitted from the Emergency Department from April 2011 to September 2012. All underwent the resuscitation protocol aimed to achieve hemodynamic goals within 6 hours after diagnosis. These goals included: 1) mean arterial >65 mmHg, 2) urine output >0.5 ml/kg/hour and 3) superior vena cava O₂ saturation >70% or serum lactate clearance >10%. The primary outcome was 28-day mortality.

**Results:** Of the 175 enrolled patients, 23 (13.1%) achieved all 3 goals at 6 hours while 75 (42.8%) achieved 2 goals and 52 (29.8%) achieved only 1 goal. The 28-day mortality of these patients was 8.7%, 16% and 33.5%, respectively while 44% of those who did not achieve any goal died. A central venous catheter was placed in 79 patients, 46 of whom had it inserted during the first 6 hours, and 42 of whom had a CVP of 8-12 mmHg. Only 13 patients had their ScvO, measured. Mean arterial pressure target was achieved in 129 patients, who had lower initial APACHE II score, lower initial lactate level and higher initial blood pressures than those who did not. These patients received less fluid at 6 hours, at 24 hours and at 3 days, respectively; they also received less norepinephrine. This group had lower mortality (28-day mortality 19.4% vs. 34.86%, p = 0.043). Of 119 patients who had achieved the urine output goal, 21 reached this goal alone and their survival was better than those who did not achieve any target goal. Serum lactate was monitored in 51 patients and a clearance of >10% was noted in 23 of them. These patients were divided into 3 groups: group 1 consisted of patients with initial lactate <2, group 2 were patients with initial lactate >2, which decreased during resuscitation; group 3 consisted of patients with initial lactate >2, which increased after wards. The mortalities were 7.7%, 14.3% and 43.6%, respectively, p = 0.011.

**Conclusion:** The achievement of therapeutic targets at 6 hours after sepsis/septic shock resuscitation was associated with improved survival, especially when more goals were reached. Although the achievement of adequate tissue oxygenation was proved beneficial, only one-third of the patients were monitored.

**Keywords:** Severe sepsis, Septic shock, Early goal-directed therapy, Goal achievement, Mortality rate

*J Med Assoc Thai 2014; 97 (Suppl. 3): S176-S183
Full text e-Journal: http://www.jmatonline.com*
Septic shock survival rate:
According to MAP at 6 hours after treatment

<table>
<thead>
<tr>
<th>MAP Range</th>
<th>Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 55</td>
<td></td>
</tr>
<tr>
<td>55-60</td>
<td></td>
</tr>
<tr>
<td>60-65</td>
<td></td>
</tr>
<tr>
<td>65-70</td>
<td></td>
</tr>
<tr>
<td>70-75</td>
<td></td>
</tr>
<tr>
<td>&gt; 75 mmHg</td>
<td></td>
</tr>
</tbody>
</table>
Septic shock survival rate:
According to urine output at 6 hours

Survival rate

Urine output ranges from Urine<0.25 to >1.5 ml/kg/hr.
Goals achievement and septic shock outcome

Table 3. Resuscitation goals at 6 hours and outcomes

<table>
<thead>
<tr>
<th>Outcomes/ goal achievement</th>
<th>No goal (n = 25)</th>
<th>Blood pressure (n = 31)</th>
<th>Blood pressure and urine output (n = 75)</th>
<th>Blood pressure and urine output and lactate(n = 23)</th>
<th>Urine output (n= 21)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>28 days mortality (%)</td>
<td>44</td>
<td>35.5</td>
<td>16</td>
<td>8.7</td>
<td>23.8</td>
<td>0.008</td>
</tr>
<tr>
<td>Hospital mortality (%)</td>
<td>48</td>
<td>41.9</td>
<td>18.7</td>
<td>8.7</td>
<td>28.6</td>
<td>0.003</td>
</tr>
<tr>
<td>ICU LOS only 48 pts (days)</td>
<td>16.2±13.9</td>
<td>20.1±25.0</td>
<td>5.7±4.7</td>
<td>5.8±5.0</td>
<td>61.5±58.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>24.5±21.9</td>
<td>31.0±30.0</td>
<td>19.0±16.5</td>
<td>23.5±30.7</td>
<td>28.6±22.1</td>
<td>0.34</td>
</tr>
<tr>
<td>Survival days without venti</td>
<td>11.9±13.4</td>
<td>14.7±12.8</td>
<td>21.9±9.6</td>
<td>22.1±9.7</td>
<td>17.8±13.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>lator in the 1st 28 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Survival days without vaso</td>
<td>16.0±12.1</td>
<td>18.0±11.8</td>
<td>23.4±7.5</td>
<td>23.1±7.8</td>
<td>19.1±10.5</td>
<td>0.006</td>
</tr>
<tr>
<td>pressor in the 1st 28 days</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Treatment outcomes from patients who achieved treatment goal at 6 hours were evaluated. One-way ANOVA was used to compare the continuous variables and Chi-square test was used to compare the categorical variables of 5 groups.
High versus Low Blood-Pressure Target in Patients with Septic Shock

- Include 776 severe sepsis/septic shock patients
  - Mean ABP = 74 mmHg
  - Mean HR = 104/min
  - Lactate = 3.7 mmol/L
  - Received fluid 2,900 mL
  - Norepinephrine 94%

- Randomized into
  - Low mean ABP > 65 mmHg
  - High mean ABP > 80 mmHg

- Low BP VS High BP
  - 28d mortality 34 vs 36.7, P=0.57
  - 90d mortality 42.3 vs 43.8, P=0.74
  - Median dose NE 0.45 vs 0.58, P<0.001
  - Renal replacement 35.8 vs 33.5, P=0.5
  - RRT in chronic HT 42.2 vs 31.7, P=0.046
The 5th study

To evaluate the impact of direct ICU admission and septic shock outcome

- Prospective study
  - Included 175 severe sepsis and septic shock patients
  - 50 patients were immediately admitted to ICU
  - 28d mortality
  - ICU vs Non-ICU
  - 18 vs 25.6%, P=0.33
Identify problem

Review literature

Apply to our system

Reevaluate

Known our nature
Septic shock guideline
Septic shock guideline

- To improve quality of patient care
- To improve outcomes of severe sepsis and septic shock patients
- To promote research in septic shock management
Septic shock guideline

- Diagnostic criteria
- Source identification and control
- Specimen collection
- Antibiotic guideline
- Hemodynamic management guideline
- Perioperative care
Septic shock guideline

- Source identification + control
  - Early appropriate antibiotic
  - Adequate drainage

- Hemodynamic management

- Organ and metabolic support
Source identification and control

- **Urinary tract infection:** 26.9%
  - Pyelonephritis
- **Respiratory tract infection:** 25.7%
  - Pneumonia
- **Intra-abdominal infection** 17.1%
  - Hepatobiliary tract infection
  - Peritonitis
  - Perforation of holo viscous organ
- **Skin and soft tissue infection** 8.6%
- **Primary bacteremia** 22.9%
Septic shock guideline

Lactate

Septic shock guideline

Lactate
Hemodynamic management

1. Adequate volume
   - No: Invasive monitoring (CVP or PCWP)
   - Yes: Acceptable BP

2. Acceptable BP
   - No: Urine > 0.5 ml/kg/hr
     - Yes: Serum lactate, SVC O₂ sat ≥ 80%
     - Yes: SVC O₂ sat or mixed venous O₂ sat ≥ 70%

3. Adequate perfusion
   - No: MAP < 65 mmHg, use vasopressor
     - No: MAP > 90 mmHg, titrate vasopressor

Options:
- Norepinephrine 0.02-2 ug/kg/min
- Dopamine 5-15 ug/kg/min
- Hydrocortisone 50 mg IV drip for 6 days
- Adrenaline drip titrate dose

Conditions:
- Hct < 30%: Hct ≥ 30%
- Hct > 30%: Dobutamine 5-20 ug/kg/min
Mortality rate of septic shock patients admitted in Siriraj Medical Units

Septic shock guideline

Severe sepsis/septic shock
Only 28% of pts with MAP < 65 mmHg had CVP monitoring at 6 hrs

Urine > 0.5ml/kg/hr in 60% of pts

ScvO₂ was evaluated in 6% of pts

Lactate was measured in 70% of pts
Can we further improve patient’s outcome?

- Direct ICU admission may improve septic shock patients outcome
- What things make it difference?
- ICU admission patients received more
  - Fluid in 1\textsuperscript{st} day: 5.7±2.0 vs. 5.0±1.7 L, \(P = 0.04\)
  - Norepinephrine: 88\% vs. 68\%, \(P = 0.007\)
  - Dobutamine: 20\% vs. 4.8\%, \(P = 0.003\)
  - Renal replacement: 28\% vs. 5.6\%, \(P < 0.001\)
Surviving Sepsis Campaign: 2012

- Fluid therapy for severe sepsis/septic shock
  - Initial fluid challenge to achieve a minimum of 30 mL/kg of crystalloids
  - Crystalloid as the initial fluid of choice
    - Against the use of hydroxyethyl starches
    - Albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids
  - Fluid challenge technique
Early goal directed therapy (EGDT)

• Multicenter RCT in USA
  – Included 1,341 severe sepsis/septic shock
    • Age 60 year-old
    • APACHE II 20.7
    • Hypotension 50%
    • Systolic BP 100 mmHg
    • Baseline lactate 4.9 mmol/L
  – Randomized into 3 groups
    • EGDT (CVP, ScvO₂, dobutamine)
    • Standard care
    • Usual care

Figure S1. – Protocol for early goal-directed therapy (EGDT).
A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

**Standard therapy**

- **Multicenter RCT in USA**
  - Included 1,341 severe sepsis/septic shock
    - Age 60 year-old
    - APACHE II 20.7
    - Hypotension 50%
    - Systolic BP 100 mmHg
    - Baseline lactate 4.9 mmol/L
  - Randomized into 3 groups
    - EGDT (CVP, ScvO₂, dobutamine)
    - Standard care
    - Usual care
A Randomized Trial of Protocol-Based Care for Early Septic Shock

The ProCESS Investigators*

• Outcome
  – EGDT vs standard vs usual
  – 60d mortality  21 vs 18.2 vs 18.9,  P=0.84
  – 90d mortality  31.9 vs 30.8 vs 33.7, P=0.66
  – CVS failure    61.3 vs 63.7 vs 56.1, P=0.06
  – Respiratory   38 vs 36.5 vs 32.4,  P=0.19
  – Renal         3.1 vs 6.0 vs 2.8,   P=0.04
The following fluid

<table>
<thead>
<tr>
<th>Time</th>
<th>Fluid Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st hr</td>
<td>600-800 mL</td>
</tr>
<tr>
<td>6th hr</td>
<td>2-3 L</td>
</tr>
<tr>
<td>24th hr</td>
<td>5-6 L</td>
</tr>
<tr>
<td>D2</td>
<td>1.5-2 L</td>
</tr>
<tr>
<td>D3</td>
<td>1-1.5 L</td>
</tr>
</tbody>
</table>
Continuing studies

• Does early norepinephrine administration could decrease mortality in severe sepsis and septic shock patients compare with conventional treatment?

• Efficacy of corticosteroid in the severe sepsis with ARDS patients?

• Colloid versus crystalloid in shock resuscitation

• Extracorporeal organ support and the outcome of septic shock with multiple organ failure