Guideline Updates
Sepsis, Surgical Site Infection (SSI), and Targeted Temperature Management (TTM)

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*I have nothing to disclose regarding this presentation

Presentation Objectives
• Review the key changes/new recommendations to the guidelines for sepsis, SSI, and TTM
• Evaluate the supporting evidence for these changes and new recommendations
• Discuss the potential impact on current practice

Surviving Sepsis Guidelines

Updated Version: 2016
Updated Version: 2016

2012
Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Severe Sepsis and Septic Shock: 2012

2012

Definitions

2016: Sepsis-3
2012: SIRS

Sepsis
Life-threatening organ dysfunction caused by a dysregulated host response to infection

Severe Sepsis
Sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion

Septic Shock
Sepsis-induced hypotension persisting despite adequate fluid resuscitation

Identification of Sepsis

2016
1. Continue screening and early identification of sepsis as previously recommended
2. First step is identification of infection then screen for organ dysfunction/high risk of deterioration using qSOFA

qSOFA (Score ≥2)
Altered mental status (GCS <13)
RR ≥22
Systolic BP ≤100

Initial Resuscitation

2016
1. Resuscitation should begin immediately
2. At least 30 mL/kg of IV crystalloid within 3 hours
3. Dynamic over static variables to predict fluid responsiveness
4. Initial target MAP of 65 mmHg
5. Normalize lactate

2012: EGDT
1. Protocolized resuscitation – Goals during first 6 hours:
   • CVP 8-12 mmHg
   • MAP ≥ 65 mmHg
   • Urine output ≥0.5 mL/kg/hr
   • Scv2 of 70% or Svo2 of 65%
2. Normalize lactate

EGDT = early goal-directed therapy; CVP = central venous pressure; MAP = mean arterial pressure; ScvO2 = superior vena cava oxygenation saturation; Svo2 = superior vena cava oxygen saturation
### ARISE, ProCESS, and ProMISe

<table>
<thead>
<tr>
<th>Study</th>
<th>Intervention</th>
<th>Mortality Outcome(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rivers et al</td>
<td>EGDT for 24 hours vs standard care (n=263)</td>
<td>In hospital: 30.5% vs 44.9%, p=0.009 28-day: 33.2% vs 49.2%, p=0.01 60-day: 44.3% vs 66.9%, p=0.03 In hospital: 14.5% vs 17.7%, p=0.53 90-day: 18.8% vs 18.8%, p=0.90</td>
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<tr>
<td>ARISE</td>
<td>EGDT for 6 hours vs standard care (n=1600)</td>
<td>In hospital: 21.0% vs 16.7%, p=0.04 90-day: 31.9% vs 33.9%, p=0.42 In hospital: 25.6% vs 24.4%, p=0.74 90-day: 29.8% vs 29.2%, p=0.90</td>
</tr>
<tr>
<td>ProCESS</td>
<td>EGDT vs protocolized standard care (6 hours) vs standard care (n=341)</td>
<td></td>
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<tr>
<td>ProMISe</td>
<td>EGDT for 6 hours vs standard care (n=1260)</td>
<td></td>
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</tbody>
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### Hemodynamic Monitoring

**Static Variables**
- MAP goal: 65 mm Hg

**Dynamic Variables**
- No difference in mortality
- Increased rate of atrial fibrillation

**SEPSIS-5**
- Higher MAP goal (80-85) associated with:
  - No difference in mortality
  - Increased rate of atrial fibrillation

### Fluid Therapy

**FEAST Trial**
- Mortality reduced in control group
  - Albumin bolus: 10.6%, p=0.03
  - Saline bolus: 10.5%
  - No bolus: 7.3%
- Give additional fluid cautiously as patient stabilizes

**Balanced Crystalloids**
- versus

**Saline**

### Antibiotics – Combination Therapy

**2016**
- 1. Suggested for the initial management of septic shock
- 2. Not recommended for other serious infections including bacteremia, sepsis without shock, and neutropenic sepsis
- 3. De-escalate within the first few days in response to improvement

**2012**
- 1. Suggested for neutropenic patients with severe sepsis and for suspected multi-drug resistant pathogens
- 2. For patients with septic shock and P. aeruginosa and S. pneumoniae bacteremia
- 3. Should not be used empirically for > 3-5 days

### Combination Therapy (CT)

- Meta analysis of monotherapy (MT) vs CT in d2 trials → sepsis/septic shock (n=8,504)
- Incidence of AKI (RIFLE): 8.4% vs 14%; p<0.001
- Renal replacement therapy: 6.3% vs 10%; p=0.005
- No overall mortality benefit (OR 0.85; p=0.09)
- Mortality in APACHE II > 21 (OR 1.53; p=0.003)
- Mortality in APACHE II 5-20 (OR 1.53; p=0.003)
- Renal replacement therapy: 6.3% vs 10%; p=0.005
- More ICU free days (11.3 vs 3.2; p=0.0002)
- More ventilator free days (12.5 vs 5.5; p<0.002)
- CT only used in 28.3% of patients but significant reduction in mortality (54% vs 49%; p=0.042)

**Intervention**
- Meta analysis of monotherapy (MT) vs CT in d2 trials → sepsis/septic shock (n=8,504)

**Outcome(s)**

- No overall mortality benefit (OR 0.85; p=0.09)
- Mortality in APACHE II > 21 (OR 1.53; p=0.003)
- Mortality in APACHE II 5-20 (OR 1.53; p=0.003)
- More ICU free days (11.3 vs 3.2; p=0.0002)
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**Before/After study of MT vs CT → ICU patients with severe sepsis/septic shock (n=1,372)**

**Kumar et al.**

**De Manning et al.**

**Dias et al.**

**Antibiotics – Procalcitonin**

2016

1. Suggest procalcitonin levels to support discontinuation of antibiotics in patients who appear septic but have limited evidence of infection

2. New: Suggest use of procalcitonin levels to support shortening duration of antibiotic therapy in sepsis

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**Conclusions**

- New definitions reflect increased understanding of sepsis
- qSOFA score helps identify patients with highest risk of deterioration
- Early goal directed therapy and CVP/ScvO₂ monitoring are no longer recommended
- Emphasis on early recognition and rapid initiation of key therapies such as fluids, LR, saline, or plasma-lyte, and antibiotics
- Dynamic monitoring variables should be used to prevent over administration of fluids
- Consider empiric antibiotic combination therapy for septic shock
- Procalcitonin levels can assist with shortening antibiotic durations

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**Surgical Site Infection Guidelines**

Updated Version: 2017

Previous Version: 1999

**Parenteral Antibiotics**

2017

1. Maintain therapeutic levels in serum/tissue throughout the operation until incision closure

2. In clean and clean-contaminated procedures do not give additional doses after incision is closed, *even in the presence of a drain*
Parenteral Antibiotics

Mayer et al
- RCT in radical gynecologic surgery (n=66)
- 1 vs 3 doses of piperacillin + tazobactam
- No complications in 48% vs 43% of patients; p>0.05

Meta analysis
- Included 21 RCTs of various surgery types (n=14,285)
- Post-operative antibiotic dosing vs placebo
  - SSI: OR 1.19; p=0.15

Berrios-Torres SI, et al.
Mayer HO, et al.

For high risk cesarean section administer antibiotic after the umbilical cord is clamped

Administer antibiotics before skin incision in all cesarean section procedures

Meta Analysis of 7 RCTs (n=2,493)
- No difference: Incisional SSI: OR 0.82; p=0.41
- Neutonatal sepsis: OR 0.81; p=0.47

Benefit with prior to incision:
- Endometritis: OR 0.57; p=0.03

Non-Parenteral Antimicrobials

2017: New
1. Do not apply antimicrobial agents to the surgical incision for prevention of SSI
2. Application of autologous platelet-rich plasma is not necessary
3. Consider triclosan-coated sutures
4. Application of a microbial sealant for skin preparation is not necessary
5. Consider intraoperative irrigation of deep or subcutaneous tissues with aqueous iodophor solution

Operative Temperature Management

2017
- New: Maintain perioperative normothermia
- RCT of patients undergoing minor elective surgery
  - Standard treatment
  - Local warming (heat dressing)
  - Systemic warming (heat blanket)
- RCT of patients undergoing elective abdominal surgery
  - Warming mattress (40°C)
  - 2 hours before and 2 hours after
- SSI rate lower in both warming groups (18% vs. 14%)
- SSI rate lower extended warming group (12.8% vs. 26.7%)

Operative Glucose Management

2017
- Implement glycemic control with a target of 200 mg/dL in diabetic and non-diabetic patients

1999
- Control serum glucose levels in all diabetic patients

Gandhi et al
Berrios-Torres SI, et al.

Conclusions
- Antiseptic agents for skin preparation should be alcohol based
- In cesarean section antibiotics should now be given prior to skin incision
- Clean and clean-contaminated procedures do not require post-operative antibiotic prophylaxis
- Evidence to support use of non-parenteral antimicrobials is inconclusive
- Perioperative management should include control of glucose and use of warming measures to avoid hypothermia
Targeted Temperature Management (TTM) Guidelines

Neurocritical Care Society (NCS): 2017

The Implementation of Targeted Temperature Management: An Evidence-Based Guideline from the Neurocritical Care Society


OHCA = out of hospital cardiac arrest; TBI = traumatic brain injury; ICP = intracranial pressure; HIE = hypoxic-ischemic encephalopathy

Laish-Farkash et al

51 comatose VF arrest patients → TTM
Goal temp 32-34°C using external cooling
Favorable outcome: 21 vs 17 hours; p=0.046

Jiang et al

215 severe TBI patients → TTM
TTM: Long term (5) vs short term (2) days
Favorable outcome: 43.5% vs 29.0%; p<0.05

Cooling Methods and Monitoring


50 patients assigned to mild hypothermia (33°C) or normothermia (37°C)
10 patients in each group:
- Conventional cooling (ice/cold packs)
- Water circulating blanket
- Air circulating blanket
- Gel pads
- Intravascular cooling

Outcome(s)
Temperature decline:
- Water circulating blanket: 1.33 °C/hr
- Gel-pads: 1.04 °C/hr
- Intravascular cooling: 1.46 °C/hr

Significantly lower
Conventional cooling: 0.31 °C/hr
Air circulating blanket: 0.18 °C/hr
p<0.01

Shivering


Bedside Shivering Assessment Scale (BSAS)
0 = none: No shivering
1 = Mild: Shivering of neck/thorax: artifact on ECG or felt by palpation
2 = Moderate: Involvement of upper extremities +/- thorax
3 = Severe: Sustained upper/lower extremities or generalized shivering

May et al → BSAS correlated with dEMG
Dressler et al → High interrater reliability of BSAS
Adverse Effects

Pharmacokinetics

Conclusions

Guideline Updates

Reduced intestinal drug absorption and delayed gastric emptying
Kaufmann et al. lower plasma concentrations of clopidogrel in cardiac arrest patients undergoing TTM

Reduced hepatic drug metabolism
Bjelland et al. lower clearance of fentanyl, morphine, and propofol in TTM patients
Fukuoka et al. half-life of midazolam prolonged and higher serum concentrations
Caldwell et al. decreased clearance of vecuronium

Conclusions

• Longer cooling durations are associated with improved outcomes in cardiac arrest and TBI
• Methods of cooling such as surface, intravascular, and cold saline shorten time to target temperature
• Intravascular catheters help maintain a more constant temperature
• Use a shivering assessment tool such as BSAS to guide therapy
• Establish a step-wise protocol for treatment of shivering
• Monitor for known adverse effects during TTM
• Consider drug level monitoring during TTM if possible
• Patients may require lower doses of sedative/pain medications

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