Do Campaigns Result In Quality Improvement?

Andrew Rhodes

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Objectives: To provide an update to the ‘Surviving Sepsis Campaign Guidelines for Management of Severe Sepsis and Septic Shock’ last published in 2008.

Design: A consensus committee of 68 international organizations was convened. Nominal groups were assembled at key international meetings for those committee members attending the conference. A formal conflict of interest policy was developed at the outset of the process and enforced throughout. The entire guidelines process was conducted independent of any industry funding. A stand-down meeting was held to identify general guidelines, IIV and sub-chapters, and selected individuals. Teleconferences and electronic-based discussion among subgroups and among the entire committee-based on the draft of the guidelines.

Methods: The authors were asked to follow the principles of the Guideline of Recommendations Assessment, Development, and Evaluation (GRADE) system to guide assessment of quality of evidence from high to low and to determine the strength of recommendations as strong to weak. The potential for bias in making recommendations in the presence of low-quality evidence was emphasized. Some recommendations were upgraded QG. Recommendations were classified into three levels: level 1 (directly targeting severe sepsis) or three level 2 (indirectly targeting severe sepsis) or level 3 (pediatric considerations).

Results: Key recommendations are listed in the table. This document is intended to include only consensus recommendations of the entire patient during the need for recognition of the (ICU). Institutional.
We recommend the **protocolized**, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion. During the first 6 hours of resuscitation, the **goals of initial resuscitation should include all** of the following as a part of a treatment protocol (grade 1C):

a) CVP 8–12 mm Hg  
b) MAP ≥ 65 mm Hg  
c) Urine output ≥ 0.5 mL/kg/hr  
d) Scvo2 ≥ 70%.
SSC 2012 Resuscitation Bundle

SURVIVING SEPSIS CAMPAIGN CARE BUNDLES

TO BE COMPLETED WITHIN 3 HOURS:
1) Measure lactate level
2) Obtain blood cultures prior to administration of antibiotics
3) Administer broad spectrum antibiotics
4) Administer 30 mL/kg crystalloid for hypotension or lactate ≥ 4 mmol/L

TO BE COMPLETED WITHIN 6 HOURS:
5) Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥ 65 mm Hg
6) In the event of persistent arterial hypotension despite volume resuscitation (septic shock) or initial lactate ≥ 4 mmol/L (36 mg/dL):
   - Measure central venous pressure (CVP)*
   - Measure central venous oxygen saturation (ScvO₂)*
7) Remeasure lactate if initial lactate was elevated*

*Targets for quantitative resuscitation included in the guidelines are CVP of ≥8 mm Hg, ScvO₂ of ≥ 70%, and normalization of lactate.
Background of Resuscitation Bundle

- Landmark trial by Rivers in 2001
- Single-centre design RCT
  - N=263
- Randomized EGDT vs. usual care
- 16% Absolute Mortality reduction
  - 30 vs. 46%
Rivers Protocol

1. Supplemental oxygen ± endotracheal intubation and mechanical ventilation
2. Central venous and arterial catheterization
3. Sedation, paralysis (if intubated), or both

- **CVP**
  - < 8 mm Hg: Crystalloid
  - 8–12 mm Hg: Crystalloid, Colloid
  - > 12 mm Hg: MAP

- **MAP**
  - < 65 mm Hg: Vasoactive agents
  - > 90 mm Hg: No further intervention

- **ScvO2**
  - < 70%: Transfusion of red cells until hematocrit > 30%
  - > 70%: Inotropic agents

- Goals achieved:
  - No: Early insertion of ScvO2 catheter
  - Yes: Hospital admission

**Therapy titrated to CVP, MAP and ScvO2**

**Potential for RBC and Inotropes**
Questions still to be answered from Rivers..

• Is the difference due to protocolized care?

• Is it necessary to use all elements of the protocol?
  – Controversial aspects include:
    • Early CVP line insertion
    • ScvO2 monitoring, which drives RBC and inotropes

• Are the results generalizable?
  – In 2014 where we have SSC +
    • With current practices
    • In a multi-centric design
In the last 12 months there have been 3 RCTs published in the NEJM repeating this work.

- ProCESS / ARISE / Promise
- Each of these essentially repeats the Rivers work, but
  - In a multi-centric design
  - In a group of patients with a better outcome
- None of them have been able to repeat the findings of improved outcomes with this protocolized methodology.
Caveats / Limitations of ProCESS, ARISE & Promise

• Usual care was usual care when shock was recognized
  – It did not test.
    • Early versus late recognition
    • Prompt versus late treatment

• Therefore these studies do not undermine efforts to

• These studies were not a repeat of the Rivers study
  – Single versus multi-centric
  – Late 1990s versus 2008-13
Change in Compliance Over Time

St George’s University Hospitals NHS Foundation Trust, Critical Care Directorate
Mortality of Sites During Campaign

Mortality over 4 year study period
- 36.7% to 27.5%
- ARR: 9.2% and **RRR: 25.0%**
- \( p=0.005 \)
Surviving Sepsis Campaign: Association Between Performance Metrics and Outcomes in a 7.5-Year Study

Mitchell M. Levy, MD, FCCM; Andrew Rhodes, MB BS, MD (Res); Gary S. Phillips, MAS; Sean R. Townsend, MD; Christa A. Schorr, RN, MSN; Richard Beale, MB BS; Tiffany Osborn, MD, MPH; Stanley Lemeshow, PhD; Jean-Daniel Chiche, MD; Antonio Artigas MD, PhD; R. Phillip Dellinger, MD, FCCM

TABLE 4. Odds of Hospital Mortality for Site Quarter of Participation, Resuscitation Bundle Compliance, and Management Bundle Compliance for Two Logistic Regression Models

<table>
<thead>
<tr>
<th>Model</th>
<th>Risk factors</th>
<th>OR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Continuous compliance, either resuscitation or management bundle,</td>
<td>For every additional quarter of site participation</td>
<td>0.96 (0.95–0.97)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>as a site-level variable and measured in last 2 quarters of site's</td>
<td>10% increase in resuscitation compliance</td>
<td>0.95 (0.94–0.97)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SSC participation</td>
<td>10% increase in management compliance</td>
<td>0.97 (0.96–0.98)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>2. Compliance as a patient-level variable and measuring whether</td>
<td>For every additional quarter of site participation</td>
<td>0.97 (0.96–0.98)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>patient's ICU visit was compliant with resuscitation or with</td>
<td>Resuscitation compliance, yes vs. no</td>
<td>0.82 (0.76–0.88)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>management bundle</td>
<td>Management compliance, yes vs. no</td>
<td>0.76 (0.71–0.81)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>
The IMPRESS-SSC Study
An International Multi-Centre Prevalence Study of Sepsis

Top Countries
1. USA
2. United Kingdom
3. Malaysia
4. Spain
5. India
6. Italy
7. China
8. Brazil
9. Greece
10. Belgium

November 7th 2013
62 Countries from all continents
1794 Patients
The IMPRESS-SSC Study
An International Multi-Centre Prevalence Study of Sepsis

<table>
<thead>
<tr>
<th>3 Hour Bundle Compliance</th>
<th>19% Overall Compliance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measurement of Lactate</td>
<td>56</td>
</tr>
<tr>
<td>Obtain Blood Cultures Prior to Antibiotics</td>
<td>49</td>
</tr>
<tr>
<td>Administer Broad Spectrum Antibiotics</td>
<td>64</td>
</tr>
<tr>
<td>Administer 30 mL/kg crystalloid for hypotension</td>
<td>57</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>6 Hour Bundle Compliance</th>
<th>36% Overall Compliance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apply vasopressors</td>
<td>66</td>
</tr>
<tr>
<td>Measure CVP</td>
<td>57</td>
</tr>
<tr>
<td>Measure ScvO2</td>
<td>47</td>
</tr>
</tbody>
</table>
Hospital Mortality (%) by Bundle Compliance

**3 Hour Bundle**

- Compliant: [Bar Chart]
- Non compliant: [Bar Chart]

**6 Hour Bundle**

- Compliant: [Bar Chart]
- Non compliant: [Bar Chart]

P<0.001
### Relationship Between Bundle Compliance and Outcome.

GEE population-averaged logistic regression model adjusted hospital mortality odds ratios

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hospital mortality odds ratio(^1)</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full 3 hour bundle</td>
<td>0.70</td>
<td>0.51 – 0.96</td>
<td>0.026</td>
</tr>
<tr>
<td>Full 6 hour bundle</td>
<td>0.75</td>
<td>0.58 – 0.96</td>
<td>0.020</td>
</tr>
</tbody>
</table>

\(^1\)Adjusted for ICU admission, sepsis status (severe vs. shock), location (ED, ward, ICU, OR, unknown), and APACHE II
Lessons from SSC Database (s)

✓ Participation alone is associated with improvement.

✓ Continued participation is associated with further benefits.
  • For every quarter, mortality reduced by 1%

✓ Higher compliance was associated with:
  • Even greater mortality reductions
  • Reduced use of resources
Summary

- Resuscitation of patients with sepsis should be initiated as soon as hypoperfusion is recognized and should not be delayed pending ICU admission.

- The goal of resuscitation is to restore tissue perfusion within the first 6 hours (Best practice statement), reasonable goals may include:
  - CVP 8–12 mm Hg (if available),
  - MAP ≥ 65 mm Hg,
  - urine output ≥ 0.5 mL/kg/hr,
  - and resolution of clinical signs of hypoperfusion (including altered mental status, mottled skin, and oliguria).
Summary

• Frequent assessment of the patients’ volume status is crucial throughout the resuscitation period.

• We suggest targeting resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion (grade 2C).

• We do not suggest routine measurement of Scvo2 or Svo2 to guide therapy during resuscitation of patients with sepsis and hypoperfusion (grade 2B).
Thank You!
New Bundles & CMS “Core Measures” to Begin October 2015
NQF BUNDLE: Sepsis 0500

TO BE COMPLETED WITHIN 3 HOURS OF TIME OF PRESENTATION†:

1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30ml/kg crystalloid for hypotension or lactate ≥4mmol/L

† “time of presentation” is defined as the time of triage in the Emergency Department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements severe sepsis or septic shock ascertained through chart review.
NQF BUNDLE: Sepsis 0500

TO BE COMPLETED WITHIN 6 HOURS OF TIME OF PRESENTATION:

5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP) ≥65mmHg

6. In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was ≥4 mmol/L, re-assess volume status and tissue perfusion and document findings according to table 1.

7. Re-measure lactate if initial lactate elevated.
NQF BUNDLE: Sepsis 0500

DOCUMENT REASSESSMENT OF VOLUME STATUS AND TISSUE PERFUSION WITH:

EITHER

• Repeat focused exam (after initial fluid resuscitation) including vital signs, cardiopulmonary, capillary refill, pulse, and skin findings.

OR TWO OF THE FOLLOWING:

• Measure CVP
• Measure ScvO2
• Bedside cardiovascular ultrasound
• Dynamic assessment of fluid responsiveness with passive leg raise or fluid challenge