Sepsis Wave II
Fluid and Pressors Management
Challenging Cases and Exceptions
Presenters

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DISCLOSURES:
- None

DISCLAIMER UPDATES:
- Verdict on fluids still pending
- Expert opinion replaced with growing evidence base
- See attached references
E-QUAL SEPSIS INITIATIVE

OBJECTIVES

▸ SEP-1 data review
  ▸ Mortality and exclusions

▸ Surviving Sepsis Guidelines Update

▸ Evidence (or lack of) for liberal fluid use

▸ Thinking about precision medicine and patient centered care

▸ Attention to High Risk Populations

▸ Goals of Care

SEP-1 ACEP DATA

SEP-1 Mortality Rate Trend for Eligible Population:

<table>
<thead>
<tr>
<th></th>
<th>Q4 2015</th>
<th>Q1 2016</th>
<th>Q2 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Delta</td>
<td>8.5%</td>
<td>8.8%</td>
<td>8.3%</td>
</tr>
<tr>
<td>Passed</td>
<td>21.3%</td>
<td>23.0%</td>
<td>21.4%</td>
</tr>
<tr>
<td>Did Not Pass</td>
<td>29.6%</td>
<td>31.8%</td>
<td>29.7%</td>
</tr>
</tbody>
</table>
SEP-1 ACEP DATA

SEP-1 and Mortality Comparisons by Pass Rate Percentiles (2015Q4 - 2016Q2)
“As clinicians, we are bound to deviate from guidelines when such deviation is reasonably expected to improve an individual patient outcome. As clinical scientists, we are bound to evaluate the prevailing standard against emerging alternatives. These three imperatives are inseparable. We therefore caution against any quality metric or reimbursement policy that mandates slavish adherence to a particular recommendation.”
SURVIVING SEPSIS CAMPAIGN GUIDELINES

**Application of Fluid Resuscitation in Adult Septic Shock**

- Sepsis-induced hypotension or lactate ≥ 4 mmol/L (Based on SSC bundle and CMS threshold)
- Pneumonia or ALI with high flow oxygen requirements
- ESRD on hemodialysis or CHF

**Rapid infusion of 30 mL/kg Crystalloid**

- Not intubated/mechanically ventilated
- Intubated/mechanically ventilated

**Consider intubation/mechanical ventilation to facilitate 30 mL/kg crystalloid**

**Total of 30 mL/kg with frequent reassessment of oxygenation**

*Administer 30 mL/kg crystalloid within first 3 hours*

**Considerations post 30ml/kg crystalloid infusion**

1. Continue to balance fluid resuscitation and vasopressor dose with attention to maintain tissue perfusion and minimize intravascular fluid overload.
2. Implement some combination of the list below to aid in further resuscitation choices that may include additional fluid or inotrope therapy
   - Blood pressure/heart rate response
   - Urine output
   - Cardiac output
   - CVP, SwCO2
   - Pulse pressure variation
   - Lactate clearance/normalization
   - Dynamic measurement such as response of flow to fluid bolus or passive leg raising
3. Consider albumin fluid resuscitation, when large volumes of crystalloid are required to maintain intravascular volume.

**Fig. 2** This figure explores the nuancing of initial administration of 30 mL/kg crystalloid for sepsis induced hypoperfusion based on patient characteristics. It also draws attention to reassessment tools following the initial fluid dose as an influence on further fluid administration or inotropic therapy.
“Unfortunately, there is no agreed uniform definition of fluid resuscitation in the literature. Fluid administration is not necessarily the same as fluid resuscitation.”
HEART FAILURE & ESRD

- 18,122 Patients with severe sepsis
- Evaluated bundle compliance effect on mortality
- Specific attention to “CHF” and “CKD”
- Article now cited as “supportive” of aggressive treatment
Difference in fluid **0.3L**

Difference in mortality 3-4% (p<.01)

Legitimate fluids in these patients?

Misleading evidence given study population, definitions of CHF & CKD
EVIDENCE FOR FLUIDS?

Time to Treatment and Mortality during Mandated Emergency Care for Sepsis

# TIME TO TREAT:

<table>
<thead>
<tr>
<th>Subgroup</th>
<th>No. of Patients</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>49,331</td>
<td>1.04 (1.02–1.05)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>25,689</td>
<td>1.04 (1.02–1.05)</td>
</tr>
<tr>
<td>Female</td>
<td>23,634</td>
<td>1.03 (1.02–1.05)</td>
</tr>
<tr>
<td>Vasopressor use</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>16,721</td>
<td>1.05 (1.03–1.07)</td>
</tr>
<tr>
<td>No</td>
<td>32,610</td>
<td>1.02 (1.00–1.03)</td>
</tr>
<tr>
<td>Admission source</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Home</td>
<td>33,464</td>
<td>1.04 (1.02–1.05)</td>
</tr>
<tr>
<td>Other</td>
<td>15,867</td>
<td>1.04 (1.02–1.05)</td>
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<tr>
<td>Coexisting condition</td>
<td></td>
<td></td>
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<tr>
<td>Congestive heart failure</td>
<td>10,092</td>
<td>1.06 (1.04–1.09)</td>
</tr>
<tr>
<td>Hemodialysis</td>
<td>5,207</td>
<td>1.06 (1.03–1.09)</td>
</tr>
<tr>
<td>Chronic respiratory failure</td>
<td>5,738</td>
<td>1.06 (1.03–1.09)</td>
</tr>
<tr>
<td>Site of infection</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>19,839</td>
<td>1.03 (1.01–1.06)</td>
</tr>
<tr>
<td>Urinary</td>
<td>13,439</td>
<td>1.03 (1.01–1.06)</td>
</tr>
<tr>
<td>Other</td>
<td>16,055</td>
<td>1.04 (1.02–1.06)</td>
</tr>
<tr>
<td>Bacteremia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram positive</td>
<td>7,175</td>
<td>1.01 (0.98–1.05)</td>
</tr>
<tr>
<td>Gram negative</td>
<td>6,431</td>
<td>1.05 (1.01–1.09)</td>
</tr>
<tr>
<td>Other</td>
<td>965</td>
<td>1.15 (1.07–1.24)</td>
</tr>
<tr>
<td>None</td>
<td>34,757</td>
<td>1.03 (1.02–1.05)</td>
</tr>
</tbody>
</table>

Figure 2. Risk-Adjusted Odds Ratios of In-Hospital Death in the Primary Model and Prespecified Subgroups.

Shown are odds ratios, with 95% confidence intervals, for in-hospital death for each hour that it took to complete the 3-hour bundle. Other site of infection includes gastrointestinal, skin, central nervous system, and unknown.
TIME TO TREAT:

A 3-Hr Bundle

In-Hospital Mortality (%) vs. Time to Completion of 3-Hr Bundle (hr)

- Crude
- Risk adjusted
TIME TO TREAT:

C Initial Bolus of Intravenous Fluids

- Crude
- Risk adjusted

In-Hospital Mortality (%) vs Time to Completion of Bolus (hr)
FLUID RESPONSIVENESS

- Increase in SV by 10-15% in response to 250-500cc bolus
- Important to assess fluid tolerance and responsiveness before fluid loading
- Venous capacitance and myocardial dysfunction
- <40% of patients are fluid responders

REVIEW ARTICLE

A rational approach to fluid therapy in sepsis

P. Marik\(^1,\ast\) and R. Bellomo\(^2\)

\(^1\)Division of Pulmonary and Critical Care Medicine, Eastern Virginia Medical School, 825 Fairfax Av, Suite 410, Norfolk, VA 23507, USA, and \(^2\)Intensive Care Unit, Austin Health, Heidelberg, Victoria, Australia
“THE EBB AND FLOW:” THOUGHTS ON DE-RESUSCITATION

Severe Septic and Septic Shock

The Ebb Phase: Fluid Therapy
- sodium and water conservation
- hypovolemia, vasodilatation, myocardial suppression
- increase metabolic demands and impaired tissue oxygen utilization

The Flow Phase: Fluid mobilization and liberate from mechanical ventilation

Compensated Septic
- shock reversal and volume repile
- avidity for water and sodium
- low plasma oncotic pressure, increased lung water, generalized edema

Co-morbidities and Considerations:
- Incomplete source control, ongoing inflammation
  - complicated by:
  - Renal Failure, Myocardial Dysfunction
  - Liver disease, Endocrine disorder: hypothyroidism, adrenal dysfunction
  - Prolonged mechanical ventilation (increased anti-diuretic hormone)
  - Pre-existing hypertension (increased sodium and water retention)
  - Drugs: diuretics, vasodilators

Conservative Fluids and/or diuresis, renal replacement therapy
  - Closely monitor electrolytes and volume status

Persistent Ebb Phase:
- Impaired fluid mobilization

Identify and Treat Underlying Disorder
“SALT WATER DROWNING”

**CARDIOVASCULAR SYSTEM**
- Myocardial oedema ↑
- Cardiac contractility impaired
- Diastolic dysfunction
- CVP ↑ and PAOP ↑
- Venous return ↓
- SV ↓ and CO ↓
- Myocardial depression
- GSF ↓; GEDV ↓
- Pericardial effusion ↑
- CAIS ↓

**CENTRAL NERVOUS SYSTEM**
- Cerebral oedema ↑
- Impaired cognition ↑
- Delirium ↑
- Intracranial pressure ↑
- Cerebral perfusion pressure ↓
- Intracocular pressure ↑
- ICH, ICS, OCS

**RESPIRATORY SYSTEM**
- Pulmonary oedema ↑
- Pleural effusion ↑
- Altered pulmonary and chest wall compliance (cst IAP ↑)
- Impaired gas exchange:
  - Hypercapnia ↑
  - PaO₂ ↓ and PaO₂/FiO₂ ↓
- Extravascular lung water ↑
- Lung volumes ↓ (cst IAP ↑)
- Prolonged ventilation ↑
- Difficult weaning ↑
- Work of breathing ↑

**HEPATIC SYSTEM**
- Hepatic congestion ↑
- Impaired synthetic function
- Cholestasis ↑
- Impaired Cytochrome P-450 activity
- Hepatic compartment syndrome

**GASTRO-INTESTINAL SYSTEM**
- Ascites formation ↑
- Gut oedema ↑
- Malabsorption ↑
- Ileus ↑
- Abdominal perfusion pressure ↓
- Bowel contractility ↓
- IAP ↑ and APP (=MAP-IAP) ↓
- IAH and ACS ↑
- Successful enteral feeding ↓
- Intestinal permeability ↑
- Bacterial translocation ↑
- Splanchic microcirculatory flow ↓
- KGS/PDR ↓; pH ↓

**RENO SYSTEM**
- Renal interstitial oedema
- Renal venous pressure ↑
- Renal blood flow ↓
- Interstitial pressure ↑
- Glomerular filtration rate ↓
- Uremia ↑
- Renal vascular resistance ↑
- Salt retention ↑
- Water retention ↑
- Renal compartment syndrome

**ABDOMINAL WALL**
- Tissue oedema ↑
- Impaired lymphatic drainage ↑
- Microcirculatory derangements ↑
- Poor wound healing ↑
- Wound infection ↑
- Pressure ulcers ↑
- Skin oedema ↑
- Abdominal compliance ↓

**ENDOCRINE SYSTEM**
- Release pro-inflammatory cytokines ↑
  - IL-1β, TNF-α, IL-6
Severe Sepsis or Shock

Can PT tolerate 30cc/kg?

- Y: Begin standard fluid challenge
  - Patient Centered Approach
  - Early Vasopressor Use
  - Fluid substitutes
  - Micro Fluid Boluses
  - Goals of Care Discussion
  - Recognition of Exclusions

- N: Dynamic Volume Assessment
  - Micro Fluid Boluses with goal of 30cc/kg in 3 hrs
  - Balance Resuscitation With Adverse Effects
  - Recognition of Fluid Overload and Corrective Therapy

Shock?

- Y
- N

~70%
HEART FAILURE & PULMONARY HTN

- Types of heart failure
  - Systolic vs diastolic
  - Left, right and biventricular

- Beside ECHO or recent ECHO is key

- Volume responsiveness

- Considerations in right heart failure and pulmonary HTN

RIGHT HEART FAILURE & PHYSIOLOGY

- ECHO guided resuscitation
- LV only pumps what it receives
- Isolated right heart failure will not show “CHF” on CXR
- Does not respond well to aggressive fluid resuscitation
- Intubation is associated with increased mortality

Annals of Emergency Medicine, Volume 66, Issue 6, 619 - 628
Circle of Death!
RHF / PAH & SEPSIS

- Early vasopressors
  - Norepinephrine / Epinephrine
  - Vasopressin (pulmonary vasodilator)
    - Decrease RV afterload
- Dobutamine in isolation should be avoided (beneficial as combo therapy)
- Avoid phenylephrine
- May add iNO (even non ventilated patients), PDEi
RHF / PAH & INTUBATION

- **Avoid** at all costs
- Profound hemodynamic effects
  - Loss of sympathetic tone
  - Increased thoracic pressure
  - RSI medications
- Risks weighed against hypoxia & hypercarbia
- **ARDS type management** but **low PEEP**
- **NIV** is the better choice
E-QUAL SEPSIS INITIATIVE

RHF / PAH: SUMMARY

- Fluids are high risk
- Early pressors / inotropes / change HR on PPM
- Avoid hypoxia, acidosis, hypothermia
- Avoid intubation
- Pulmonary vasodilators
- ECMO / RVAD
- Goals of Care Discussions
FLUIDS & END STAGE RENAL DISEASE

- Fluid limited / restricted
- **Volume assessment / Intravascularly volume depleted**
  - fragile volume status
- **Choice of crystalloid** (NS, LR, balanced)
  - Plasmalyte / Normsol
  - Avoid large volume NS
END STAGE RENAL DISEASE: SUMMARY

- Very sick population, high mortality
- Source control
- Fluid responsiveness essential
- Early vasopressors / Dobutamine
- NIV, High Flow O2 > ETT
- Consider: Avoiding NS as crystalloid (acidemia)
CIRRHOSIS / ACLD
CIRRHOSIS: SUMMARY

- Very sick population, high mortality
- Fluid responsiveness essential
- Consider colloids (improve mortality, decrease AKI/RRT)
- Consider corticosteroids
- Early vasopressors / Vasopressin (hyporesponsive)
- Consider: Variceal bleeding & Abdominal Compartment Syndrome
GOALS OF CARE: HIGH RISK POPULATIONS

Breakdown of SEP-1 Exclusion Population:

- Did not meet Severe Sepsis Criteria: 72.9%
- Transfers: 18.0%
- Antibiotic Exclusion: 3.8%
- Comfort Care prior to or within three hours of Severe Sepsis Presentation: 2.9%
- Administrative Contraindication to Care: 1.8%
- Comfort Care prior to or within six hours of Septic Shock: 0.2%
- Expired within six hours of Septic Shock: 0.2%
- Expired within three hours of Severe Sepsis: 0.4%

Note: Cumulative data from October 2015 – March 2016
E-QUAL SEPSIS INITIATIVE

CLOSING STATEMENTS

Severe Sepsis or Shock

Can PT tolerate 30cc/kg?

Y N

Begin standard fluid challenge

Patient Centered Approach

Early Vasopressor Use

Fluid substitutes

Micro Fluid Boluses

Goals of Care Discussion

Recognition of Exclusions

Shock?

Y N

Dynamic Volume Assessment

Micro Fluid Boluses with goal of 30cc/kg in 3 hrs

Balance Resuscitation With Adverse Effects

Recognition of Fluid Overload and Corrective Therapy

~70%
FINAL THOUGHTS...

▸ Fluids are medications
▸ Become familiar with volume assessment
▸ Early pressors / inotropes
▸ Precision, patient specific management
▸ Avoid intubation / Use NIV
▸ Goals of Care Discussions
REFERENCES:


What's Next?

• Complete Sepsis Portal Activities

• Register for the June Webinar  
  www.acep.org/equal

• Questions? Contact the E-QUAL team at  
  equal@acep.org