Sepsis Survival for Patients and Nurses

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Many aspects of sepsis care have not changed

WHAT IS NOT NEW?
“Except on few occasions, the patient appears to die from the body’s response to infection rather than from it.”

— Sir William Osler, 1904

“The Evolution of Modern Medicine”
Healthy volunteer
Pathophysiology: Early Sepsis

- Myocardial Depression (early) → Hyperdynamic (late)
- Vasodilation (bigger tank)
- Capillary Leak (relative hypovolemia)
Pathophysiology: Sepsis

• Increased $O_2$ demand, decreased supply, cellular dysoxia
• Ultimately sepsis is a perfusion problem
• Code Stroke, Code STEMI… Code Sepsis!
Saying “when the SVR is high, you’re dry” is misleading.

** Fill the tank before you press on the accelerator **

Sepsis: “Relative” Hypovolemic

\[ \text{CO} = \text{HR} \times \text{SV} \]
\[ \text{MAP} = \text{CO} \times \text{SVR} \]

- Treatment:
  - Crystalloids
  - NS
  - LR
  - Albumin

** Fill the tank before you press on the accelerator **

“Teeter-Totter” Relationship

\[ \text{↑HR} \]
\[ \text{↓SV} \]
\[ \text{↑SVR} \]
\[ \text{↓CO} \]
Pathophysiology: Late Sepsis

• The only shock state that is hyperdynamic in late stages
  – Septic shock in 39 y.o. male w/ history of lupus
  – BP: 68/39
  – Central venous pressure: 15
  – Levophed 30 mcg/min
  – Phenylephrine 200 mcg/min
  – Vasopressin 0.04 u/min
Multicenter Implementation of a Treatment Bundle for Patients with Sepsis and Intermediate Lactate Values

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Abstract

Rationale: Treatments for patients with sepsis with intermediate lactate values (≥2 and <4 mmol/L) are poorly defined.

Objectives: To evaluate multicenter implementation of a treatment bundle (including timed intervals for antibiotics, repeat lactate testing, and intravenous fluids) for hemodynamically stable patients with sepsis and intermediate lactate values in the emergency department.

Methods: We evaluated patients in annual intervals before and after bundle implementation in March 2013. We evaluated bundle compliance and compared outcomes measures across groups with multivariable logistic regression. Because of their perceived risks of iatrogenic fluid overload, we also evaluated patients with a history of heart failure and/or chronic kidney disease.

Measurements and Main Results: We identified 18,122 patients with sepsis and intermediate lactate values, including 36.1% treated after implementation. Full bundle compliance increased from 32.2% in 2011 to 44.9% after bundle implementation (P < 0.01). Hospital mortality was 8.8% in 2011, 9.3% in 2012, and 7.9% in 2013 (P = 0.02). Treatment after bundle implementation was associated with an adjusted hospital mortality odds ratio of 0.81 (95% confidence interval, 0.66-0.99; P = 0.04). Decreased hospital mortality was observed primarily in patients with a history of heart failure and/or kidney disease (P < 0.01) compared with patients without this history (P > 0.40). This corresponded to notable changes in the volume of fluid resuscitation in patients with heart failure and/or kidney disease after implementation.

Conclusion: Multicenter implementation of a treatment bundle for patients with sepsis and intermediate lactate values improved bundle compliance and was associated with decreased hospital mortality. These decreases were mediated by improved mortality and increased fluid administration among patients with a history of heart failure and/or chronic kidney disease.

Keywords: hospital mortality; quality improvement; resuscitation; sepsis
Literature Review: SSC Guidelines

• “…the optimal fluid management of septic shock is unknown and currently is empirical.”

• 2008 to 2012 to 2016 SSC Sepsis Guidelines
  – Initial fluid challenge increased from 20 mL/kg to 30 mL/kg
  – “Sepsis dose” initial fluid challenge
  – 77% compliance in post-intervention group

The Bundle Has Not Changed

The Society of Critical Care Medicine has created a website:

On the Bundles tab of this website, a PDF with updated Bundles is referenced.

The PDF was revised 4/2015 by the SSC Executive Committee. It is now under revision consideration by the SSC Steering Committee based on the release of the fourth edition of the International Guidelines for Management of Sever Sepsis and Septic Shock: 2016.

Key Points from the PDF:
1. Treatment guidelines were revised 4/2015 by the SSC Executive Committee
2. Bundles have been updated in response to new evidence
3. The 6-hour SSC bundle has been updated
4. The 3-hour SSC bundle remains unchanged
Some aspects of sepsis identification and treatment are evolving

WHAT IS NEW?
The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour; Manu Shankar-Hari, MSc, MD, FFICM; Djamali Annane, MD, PhD; Michael Reinhart; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Croix; Mitchell M. Levy, MD; John C. Marshall, MD; Gordon D. Rubenfeld, MD, MSc; Derek C. Angus, MD, PhD; Frank Brun-Buisson, MD; Thomas D. Han, MD, MPH; Christian Finfer, MD, PhD; Ian Paterson, MD; Marie-Claude Martin, MD, PhD; Frank B. Quintel, MD; Mervyn Singer, MD, FRCP; for the Sepsis Definitions Task Force.
Sepsis/Severe Sepsis

• Confusing
  – Most people say “sepsis” when they mean “severe sepsis”
  – What the initial two task forces called “sepsis” is what most people call “infection”
New definitions aligned with clinical use

• Infection:
  – Routine infection without organ dysfunction

• Sepsis:
  – Infection progresses to (“infection-induced”) organ dysfunction

• Septic Shock:
  – Sepsis requiring vasopressors **AND** lactate > 2 mmol/L
On the Guidelines tab of the SSC website, a PowerPoint of the Campaign Guidelines Presentation is linked:

Slide #23 lists the members of the Expert Panel
Initial Resuscitation Recommendations Have Changed From 2012

<table>
<thead>
<tr>
<th>2012 RECOMMENDATIONS</th>
<th>2016 RECOMMENDATIONS</th>
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<td><strong>A. INITIAL RESUSCITATION</strong></td>
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| 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 ≥ 4 mmol/L). Goals during the first 6 hours of resuscitation:  
   a. Central venous pressure 8–12 mm Hg  
   b. Mean arterial pressure ≥ 65 mm Hg  
   c. Urine output ≥ 0.5 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). | 1. Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately (BPS).  
2. We recommend that, in the resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloidal fluid be given within the first 3 hours (strong recommendation, low quality of evidence).  
3. We recommend that, following initial fluid resuscitation, additional fluids be guided by frequent reassessment of hemodynamic status (BPS). Remarks: Reassessment should include a thorough clinical examination and evaluation of available physiologic variables (heart rate, blood pressure, arterial oxygen saturation, respiratory rate, temperature, urine output, and others as available) as well as other noninvasive or invasive monitoring, as available.  
4. We recommend further hemodynamic assessment (such as assessing cardiac function) to determine the type of shock if the clinical examination does not lead to a clear diagnosis (BPS).  
5. We suggest that dynamic over static variables be used to predict fluid responsiveness, where available (weak recommendation, low quality of evidence).  
6. We recommend an initial target mean arterial pressure of 65 mmHg in patients with septic shock requiring vasopressors (strong recommendation, moderate quality of evidence).  
7. We suggest guiding resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion (weak recommendation, low quality of evidence). |
Limitations of Physical Assessment and Static Variables

• Can you determine hypovolemia just by examination?
  – Not studied/included in sepsis trials

• Cap refill, cold extremities, etc. indices are the result (not predictive of hypovolemia)
  – Only tells you “point in time”
  – Secondary parameters that can be slow to change, misleading, and only indirect correlations with changes in cardiac output
Transitioning from Pressure-based Parameters to Flow-based Parameters

STATIC PARAMETERS
• E. Rivers:
  - Treating the number in isolation will kill people
  - CVP used in his control group
  - Post-mortem CVP → SV will still = Zero
Limitations of the CVP

Reporting to provider
Stroke Volume,
Stroke Volume Variation,
Cardiac Output

DYNAMIC PARAMETERS
• Administer fluid challenges as long as SV improves by ≥ 10%
Reference Ranges

- SV reference range = 50-100 mL
- SVV = < 13%
- C.I. = 2.8-4.2
- C.O. = 4-8 L/min
- FTc = 330-360 ms
- PV = 50-100 cm/s
- SvO2 = > 70%
- SvO2 = 60-80%
- SVR = 900-1600
- CVP = 2-8 mmHg
Example of a Real Screen

Stroke Volume
Peak Velocity: 7.7
Contractility (Height)

Preload (width)

Systolic Flow Time

Peak Velocity: 82

CO: 52.3
Cl: 4.7
HR: 95

FTc: 318
Should Levophed Continue to be the First-line Vasopressor? When Should Dobutamine be Considered?

“What’s the max dose of this pressor?”
Predictive Value of SV: Fluid Administration *According to Response*
Moving Forward: Practical Applications

PASSIVE LEG RAISE
Passive Leg Raise (PLR) *

- Kollef study (N = 102; fluid challenges in 89 patients)
  - 62% sepsis
  - 67% ventilator
  - 59% vasopressors
  - “A SV ↑ induced by PLR of ≥ 15% predicted volume responsiveness with sensitivity 81%, specificity of 93%”
  - Positive Predictive Value 91%
  - Negative Predictive Value 85%
  - 46.1% of patients were volume responsive

Bedside Cardiac Ultrasound Performed at 14:00pm

- Peak Velocity (Vpk): 1.0m/s
- Cardiac Index (C.I): 2.2 L/min/m2
- Systolic Flowtime (FTc): 318ms
- Stroke Volume (SV): 60mL

Passive leg raise test: Positive
Passive Leg Raise
What is next?

CAPNOGRAPHY
Capnography: PLR-induced Changes in EtCO₂

• EtCO₂ for predicting volume responsiveness by PLR test
• Monnet et al. (2013) (N = 65)
• “A PLR-induced increase in EtCO₂ ≥ 5% predicted a fluid-induced increase in cardiac index (CI) ≥ 15% with sensitivity of 71% and specificity of 100%”
• EtCO₂ and CI predictive ability not different

Pre to Post-Fluid Challenge Capnogram
Case Studies
Conclusion
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