Sepsis Update: Focus on Early Recognition and Intervention

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Disclosures

- I have no actual or potential conflict of interest in relation to this program/presentation.
- I will not be discussing off-label use of any medication or device
Objectives

- Recognize diagnostic criteria for different categories of sepsis
- Be able to implement evidence-based treatment measures for sepsis
- Recognize controversies in sepsis care
- Recognize goals of core measures/sepsis guidelines in historical context of sepsis care

Terminology

SIRS
Systemic disease with at least 2 clinical indicators — can be infectious or noninfectious cause
- T < 96.8 or > 100.4
- HR > 90
- RR > 20
- WBC < 4000 or > 12,000 or > 10% bands

SEPSIS
SIRS with suspected or confirmed infection

SEVERE SEPSIS
Sepsis with organ dysfunction, hypoperfusion, or hypotension

SEPTIC SHOCK
Sepsis-induced hypotension in the presence of perfusion abnormalities; fluid-refractory hypotension

REFRACTORY SEPTIC SHOCK
Multi-organ system failure and hypotension refractory to fluid resuscitation and vasoactive support
Landmark EGDT Rivers 2001

Basic study info

- Random double blind
- Pts arriving at urban ER with severe sepsis
- 6hrs of early goal-directed therapy vs standard therapy before ICU admit
- In-hospital mortality as the primary efficacy outcome
- Enrolled 263 patients
What is ScvO₂?

- Mixed central venous oxygen saturation
- Objective determination of optimization of hemodynamics
- ScvO₂ = Delivery O₂ / Consumption O₂
  - Low is bad: Delivery is too low or consumption is too high
Step 1: Optimize preload to improve cardiac output

Volume resuscitation remains a mainstay of sepsis care
Ongoing Controversy

- Does CVP assess preload responsive patients and adequacy of fluid resuscitation?
  - Static indicators such as CVP have some evidence to suggest
    - Poor indicator of volume status
    - Poor predictor of fluid responsiveness
    - Trend toward venous congestion increasing the incidence of pulmonary complications
  - It has been suggested that CVP no longer be used
  - Respiratory variation in the CVP is useful for predicting fluid responsiveness in spontaneously breathing patients


Dynamic markers such as pulse pressure variation and stroke volume variation

- Stroke volume variation (SVV) is the ratio of maximal stroke volume difference
  - Pulse pressure variation covaries with SVV
  - During positive pressure ventilation, inspiration increases the intrathoracic pressure reducing the RV filling and RV output if the RV is volume/preload responsive. This causes the LV filling and LV output to decrease over successive beats
  - SVV of >15% in patients receiving a tidal volume of >8 mL/kg or an SVV of >10% in patients receiving a tidal volume of 6 mL/kg predicts preload responsiveness

- Commercially available monitors
- Sounds great but....
  - Not applicable in spontaneously breathing patients
  - Or those with atrial fibrillation or a chest wall injury

Alternative to CVP

- Passive leg raise
  - Observational
  - 109 patients
  - Assessed stroke volume using NICOM and obtained results from PLR. Fluid bolus was defined as 5 mL/kg normal saline infusion. Fluid responsiveness was defined as an increase of SV greater than 10% from baseline.
  - PLR were significantly correlated (r = 0.78, P < .001) with fluid responsiveness
  - Made it into the SEP-1 core measures


Step 2: Optimize tissue perfusion

[Diagram showing the optimization of tissue perfusion with flowchart and decision points for fluid management based on CVP and MAP values, along with indications for vasopressors and inotropic agents.]
Step 3: Evaluate ScvO2 for goal

- Do we really need to monitor ScvO2?
- Reduced mortality with targeting normalization of lactate
  - 2010 Multicenter Dutch study
  - Decrease lactate by 20% or more per 2 hours for the initial 8 hours of ICU stay; treatment team for control group had no knowledge of lactate
  - Care was similar to EGDT with CVP and MAP goals etc; measurement of ScvO2 was at the discretion of the treatment team
  - Hospital mortality was lower in the lactate group (hazard ratio, 0.61; 0.43-0.87; P = 0.006)
    - Also, inotropes stopped, weaned from mechanical ventilation and discharged from the ICU earlier

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Step 4: Transfuse to improve oxygen carrying capacity

Step 5: Optimize CO
Results of 2001 Rivers

- 263 enrolled patients
  - 130 EGDT
  - 133 to *standard therapy*
  - Baseline characteristics same
- In-hospital mortality
  - 30.5% EGDT vs 46.5% standard rx (P=0.009)
Surviving Sepsis Campaign

- Partnership of the European Society of Intensive Care Medicine and the Society of Critical Care Medicine
- Formed 2002 to address current definitions, routes to diagnosis and treatment options
- EGDT became standard of care
Current Context

- Sixteen years since EGTD
- Tremendous improvement in sepsis mortality: Currently studies see less than 20%, compared with 46.5% seen in the 2001 trial
  - Better care?
    - What is “usual care” now?
    - Other advances in critical care
  - More recognition: i.e. less sick patient population included?
  - Combination?

PROCESS, ARISE, PROMISE, AND USUAL CARE

Is EGDT still relevant?
Conclusions:

- In patients with septic shock who were identified early and received timely intravenous antibiotics and adequate fluid resuscitation, hemodynamic management with invasive monitoring according to a strict EGDT protocol did not lead to an improvement in outcome.

- It did lead to higher rates of pressors and transfusions

- So..... Why do EGTD?
Caveats to Process/Arise/Promise

- On average the patients in the EGDT group of all three trials had a ScvO2 of 70% upon initial line insertion and measurement
  - In Rivers, average initial ScvO2 was 48.6
- The intravenous-fluid volume before randomization was similar in the two groups and on average was about 2L
  - And the difference between the groups, while statistically significant, was only about 200-250mL
- Only about two thirds of patients in either group were deemed likely to be admitted to the ICU from the emergency department if they were not enrolled in the study
  - Also lower rates of chronic disease and better functional status than Rivers (particularly Process and Arise)

This means a substantial proportion of patients in the protocol groups in ProCESS, ProMISE and ARISE (just exactly how many is not clear) had met the protocol’s goals before the protocol began.

To put it another way, EGTD is now usual care
Sepsis is a syndrome with no single clinical characteristic and a heterogeneous patient population.

It remains under-recognized and under-diagnosed and continues to have a high mortality.

SEP-1 Core Measures

- All with ICD-10 Diagnosis of Severe Sepsis and Septic Shock
  - Exclusion criteria are limited
- Live October 1, 2015
- Complex
- Requiring interventions essentially identical to Surviving Sepsis Campaign (2015 update) and Sepsis Guidelines (2016 update)
Definitions (per core measures)

- **Severe Sepsis**
  - Three conditions within 6 hours of each other
  - Presence of infection/suspected infection
  - Two or more SIRS criteria
  - **One or more** signs of organ dysfunction
    - This includes hypotension ** (SBP < 90 OR MAP < 65 or decreased in SBP by more than 40 from last SBP considered normal for the patient)

- **Septic shock**
  - Meets criteria for severe sepsis **PLUS**:
    - Lactate ≥ 4
    - “Severe sepsis with hypotension not responding to administration of crystalloid fluids,” translated: Severe sepsis is present, treated with a bolus of 30mL/kg crystalloid and then there is hypotension ** in the hour following
  - OR the provider assesses septic shock

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**Lactate of 4?**

- Lactate levels of 0–2.4 mortality 4.9% (95% CI: 3.5% – 6.3%)
- 2.5–3.9 mortality 9.0% (95% CI: 5.6% – 12.4%)
- ≥4 mmol/L **28.4%** (95% CI: 21% – 36%) respectively

Core measure Requirements

- For Severe Sepsis OR Septic Shock \( \rightarrow \) 3 HOUR CLOCK for the following measures (current usual care):
  - Lactic acid collected
  - Blood cultures prior to IV antibiotics
  - Broad spectrum IV antibiotics initiated
- For Severe Sepsis with hypotension x1 OR Septic shock \( \rightarrow \) 3 HOUR CLOCK also requires:
  - Crystalloid fluid bolus of 30mL/kg of actual body weight (LR or NS)
  - To reiterate: NOT all severe sepsis, only with hypotension
- 6 HOUR CLOCK requires:
  - Repeat lactate if initial level >2
  - Septic shock and persistent hypotension require pressors

Bottom Line

The present core measures represent a shifting paradigm
1. Moving away from uniform invasive monitoring
2. Focusing on early aggressive hydration and antibiotics
3. More emphasis on less severe disease in the sepsis spectrum
There is more to good sepsis care than automatically placing a line for invasive monitoring in all patients

- Every hour of delay in antibiotics resulted in a mean 7.6% increase in mortality (range 3.6-9.9%)
- Aggressive fluid resuscitation is still considered a main stay

System Interventions: Early Recognition

- Nursing education
- Provider education
- Best practice advisory
- ART calls/Code Sepsis
BPA

- Triggers based on
  - Heart rate >110
  - Systolic blood pressure <90
  - Temperature >100.5°F or <96.8°F
  - Lactate >2
  - WBC >12,000 or <4000 or segs >10
  - RR >25 OR ABG PaCO2 <32

Sepsis Best Practice Alert
A BPA will trigger for nurses and physicians indicating the patient may have sepsis. Nurse triggers will display:
Consider possibility of severe sepsis/septic shock diagnosis and order the sepsis bundle.
And require the following acknowledgement:
- Provider notified (or)
- Currently being treated for sepsis
The physician trigger will require acknowledgement to select:
- Critical Care Severe Sepsis Bundle
- Non-Critical Care Sepsis Order Set (PCUs only)
- treatment not appropriate
System Interventions: Bundled Care

General medical unit sepsis order set

- Part of the admission order set
- Break sepsis into 1. sepsis, 2. severe sepsis, 3. severe sepsis with hypotension and 4. septic shock with specific orders for each
- Fluid resuscitation and specific notifying parameters for sepsis, severe sepsis and septic shock issues that need to lead to escalation of care

Order set (without admit, monitoring, code status orders):

- **Sepsis**
  - Admit to general adult or progressive care
  - Severe sepsis: sepsis plus end-organ damage of lactate more than 2 but less than 4, creatinine more than 1.5, urine output less than 0.5 ml/kg/hr x 2 hours, bicarbonate more than 15, platelet count less than 100,000, INR more than 1.5, PT PTT X 4, acute respiratory failure requiring a new need for invasive or non-invasive mechanical ventilation or other end-organ damage as assessed by the provider

Sepsis expanded:

- Sepsis (defined as two or more SIRS criteria (temp more than 100.9°F or less than 96.8°F, HR greater than 90, RR more than 20, WBC more than 12K or less than 4K, or, greater than 18% bands, and presence of infection/suspected infection)) Admit to general adult unit or progressive care
- Severe sepsis: sepsis plus end-organ damage of lactate more than 2 but less than 4, creatinine more than 1.5, urine output less than 0.5 ml/kg/hr x 2 hours, bicarbonate more than 15, platelet count less than 100,000, INR more than 1.5, PT PTT X 4, acute respiratory failure requiring a new need for invasive or non-invasive mechanical ventilation or other end-organ damage as assessed by the provider
- Sepsis, Shock: defined as sepsis plus Lactate more than 4, hypotension not responsive to crystalloid fluids or as determined by provider assessment.
- Requires admission to progressive care or higher.
- If admitted to ICU, order Critical Care Severe Sepsis Bundle
- Sepsis, Shock: defined as sepsis plus Lactate more than 4, hypotension not responsive to crystalloid fluids or as determined by provider assessment.
- Requires admission to critical care or higher. Strongly consider ICU.
- If admitted to ICU, order Critical Care Severe Sepsis Bundle.
Questions?

So what about quick SOFA?

- Infection and sepsis (by the 1992 definition) are often the same
- Sepsis-3 introduces qSOFA as a tool for identifying those at risk for a poor outcome; qSOFA does not define sepsis
- Score:
  - New/worsened altered mentation
  - RR ≥ 22
  - Systolic BP ≤ 100
- The presence of two qSOFA criteria is a predictor of both increased mortality and ICU stays of more than three days in non-ICU patients
- Recommend using a change in baseline of the total SOFA score of two or more points to represent organ dysfunction