

Journal Club Eastern Virginia Medical School Therapy Article

Resident: Melanie Weller

Date: 4/25/17

CITATION: Balamuth, F., et al: Protocolized Treatment is Associated with Decreased Organ Dysfunction in Pediatric Severe Sepsis

I. WHAT IS BEING STUDIED?	
1. Study Objective	Determine if treatment of children with severe sepsis with a protocolized sepsis guideline starting in the ED, leads to decreased organ dysfunction on hospital day 2.
2. Study Design	Retrospective cohort study (1/1/2012-3/31/2014) at a tertiary care children's hospital with 90,000 ED visits.
3. Inclusion Criteria	<ul style="list-style-type: none"> • Older than 56 days younger than 18 years • Meet criteria for severe sepsis/septic shock • Required PICU admission within 24 hours of ED arrival
4. Exclusion Criteria	<ul style="list-style-type: none"> • Younger 56 days • Not meet definition of severe sepsis or septic shock on initial screen or under case review of study team • Pre-existing chronic organ dysfunction
5. Interventions Compared	Utilization of protocolized sepsis guideline with physician order set in the ED-those for which the order set was utilized vs "usual care" those patients who were cared for without utilization of sepsis order set
6. Outcomes Evaluated	<u>Primary-</u> <ul style="list-style-type: none"> • complete resolution of organ dysfunction by hospital day 2 based upon international consensus criteria for sepsis-associated organ dysfunction. • (+/- CVS/resp/neurologic/renal/hepatic/hematologic dysfunction evaluated at ED arrival, hospital admission/hosp day 1 and 2).

	<u>Secondary-</u> <ul style="list-style-type: none"> • PICU and hospital LOS • ED triage to antibiotic/fluids • Need to transfer to higher level of care within 24 hours of admission • mortality
II. Are the results of the study valid	
1. Was the assignment of patients randomized?	No. physician discretion as to whether order set utilized or not-no discrete randomization
2. Was randomization concealed (blinded)?	N/A
3. Were patients analyzed in the groups to which they were randomized?	yes
4. Were patients in the treatment and control groups similar with respect to known prognostic factors?	Overall no significant difference between protocol and usual care in terms of age/sex/race/or complex chronic conditions -also, no statistical difference in ED triage level or organ dysfunction present on ED arrival
III. Did experimental and control groups retain a similar prognosis after the study started (answer the questions posed below)?	
1. Were patients aware of group allocation?	no
2. Were clinicians aware of group allocation?	Yes-retrospective review of physician determined use of protocol vs usual care
3. Were outcome assessors aware of group allocation?	yes
4. Was follow-up complete?	N/A-retrospective cohort study
IV. What were the results? Answer the questions posed below	
1. How large was the treatment effect? (Difference between treatment and control group).	<ul style="list-style-type: none"> • 121 (64%) to protocol group • 68 (38%) to usual care

	<p>For primary outcome: Protocol patients were more likely to be OD free on hospital day 2 (RR, 5.2; 95% CI, 2.5, 10.8). Adjusted odds ratio 4.2 for complete organ dysfunction resolution by hosp day 2 in protocol group</p>
<p>2. What was the estimated treatment effect at a 95% confidence interval? (Precision)</p>	<p>Multivariable logistic regression model-utilization of ED protocol was associated with resolution of organ dysfunction by hosp day 2</p> <ul style="list-style-type: none"> Adjusted odds ratio 4.2 (95% CI 1.7-10.4) (CI does not span the null OR value and therefore can be utilized as proxy for stat sig though somewhat wide.) <p>For secondary outcomes: Protocol patients had shorter PICU stays (median 69.0 vs. 196.5 hours) and had shorter hospital stays (median 140.0 vs. 347.7 hours). Mortality was not significantly different between the two groups (RR 1.1, 95% CI 0.2-5.9).</p> <p>Protocol patients had (statistically significant) shorter times to initial IV antibiotics, initial IV fluid bolus, and third IV fluid bolus compared with usual care patients. Protocol patients also received a higher total volume of fluid per kg in the ED compared with usual care patients.</p>
<p>V. Will the results help me in caring for my patients? (Applicable?)</p>	
<p>1. Were the study patients similar to my patient?</p>	<p>Yes-pediatric population with utilization of definition of pediatric sepsis guidelines</p>
<p>2. Were all clinically important outcomes considered?</p>	<p>Also evaluated in setting of mortality, timing of fluids/antibiotics-though did not fully account for improvement -did evaluate +/- central line, comorbidity as well Mortality rates reported at 3% are low compared to national and prior studies</p>
<p>3. Are the likely treatment benefits worth</p>	<p>Not specific for this article though low cost for</p>

the potential harm and costs?	institutions with EMR to create order set protocols if will decrease morbidity of sepsis.-also mentioned in paper that it may be more of a greater understanding of recognition of sepsis with introduction of protocol vs the protocol itself.
-------------------------------	---

Study Limitations

- Small number patients therefore likely underpowered to show mortality benefit as an example.
- Retrospective data analysis
- Selection bias as physicians could select who got protocol and who got usual care.
- Non-blinded including data assessors who could have been blinded
- Single center trial, tertiary academic non-community hospital setting, Patients likely to have more complex comorbidities. No mention of sources of sepsis by group.
- Unmeasured complexity of patients-making defining sepsis more challenging and therefor many have influenced physician decision to place into “usual care” group
- Misclassification bias-given protocol like treatment without using the computer based protocol
- Refer to lactate levels in “Table 1” but does not seem to have been reported.
- No economic analysis though suggested that costs in ICU and hospital days favorable impacted.

Clinical Bottom Line:

- Use of protocolized care in setting of pediatric severe sepsis/septic shock is associated with reduced organ dysfunction at hospital day 2
 - Also improved processes of care with significant impact on time to AB’s and adequate fluid resuscitation.
 - Decreased LOS in hospital and ICU.