

## The PRoCESS study

Summary by Dr. Patrick Archambault. Reviewed by Dr. Tim Chaplin & Dr. Teresa Chan.

Topic	Resuscitation / Sepsis								
Title	A Randomized Trial of Protocol-Based Care for Early Septic Shock								
Citation of Paper:	N Engl J Med. 2014 May 1; 370(18):1683-93. Epub 2014 Mar 18. PMID: 24635773								
Study Rationale	1) Is protocol-based resuscitation better to usual care ? 2) Is a protocol with central hemodynamic monitoring to guide the use of fluids, vasopressors, blood transfusions, and dobutamine ("Early Goal Directed Therapy") better than a simpler protocol that does not include these elements								
Clinical Question:	In patients with septic shock presenting to the ED, is a catheter-based goal-directed resuscitation protocol better than usual care or a simplified goal-directed resuscitation protocol?								
PICO	<table border="0"> <tr> <td>P:</td> <td>Adult septic patients in the ED with 2 SIRS criteria <b>PLUS</b> 1) refractory hypotension (SBP&lt;90 mmHg or use of vasopressors to maintain SBP &gt; 90 mHg even after 1L fluid bolus); <b>OR</b> 2) lactate level &gt; 4 mmol</td> </tr> <tr> <td>I:</td> <td>Catheter-based goal-directed sepsis protocol (see Figure S1)</td> </tr> <tr> <td>C:</td> <td>a) Simplified goal-directed sepsis protocol (see Figure S2) b) Practice as usual (no prompts by study coordinator and bedside physicians were not trained to deliver EGDT or protocol-based standard therapy)</td> </tr> <tr> <td>O:</td> <td>1) hospital mortality rate at 60 days 2) mortality rate at 90 days 3) cumulative mortality at 90 days and 1 year 4) secondary outcomes (length of cardiovascular, respiratory, renal failure, length of hospital and ICU stay, discharge disposition)</td> </tr> </table>	P:	Adult septic patients in the ED with 2 SIRS criteria <b>PLUS</b> 1) refractory hypotension (SBP<90 mmHg or use of vasopressors to maintain SBP > 90 mHg even after 1L fluid bolus); <b>OR</b> 2) lactate level > 4 mmol	I:	Catheter-based goal-directed sepsis protocol (see Figure S1)	C:	a) Simplified goal-directed sepsis protocol (see Figure S2) b) Practice as usual (no prompts by study coordinator and bedside physicians were not trained to deliver EGDT or protocol-based standard therapy)	O:	1) hospital mortality rate at 60 days 2) mortality rate at 90 days 3) cumulative mortality at 90 days and 1 year 4) secondary outcomes (length of cardiovascular, respiratory, renal failure, length of hospital and ICU stay, discharge disposition)
P:	Adult septic patients in the ED with 2 SIRS criteria <b>PLUS</b> 1) refractory hypotension (SBP<90 mmHg or use of vasopressors to maintain SBP > 90 mHg even after 1L fluid bolus); <b>OR</b> 2) lactate level > 4 mmol								
I:	Catheter-based goal-directed sepsis protocol (see Figure S1)								
C:	a) Simplified goal-directed sepsis protocol (see Figure S2) b) Practice as usual (no prompts by study coordinator and bedside physicians were not trained to deliver EGDT or protocol-based standard therapy)								
O:	1) hospital mortality rate at 60 days 2) mortality rate at 90 days 3) cumulative mortality at 90 days and 1 year 4) secondary outcomes (length of cardiovascular, respiratory, renal failure, length of hospital and ICU stay, discharge disposition)								
Methods	RCT, outcome assessment was blinded but not healthcare professionals, intention to treat analysis								
Results	1- fluid administered in the first 6 hours: EGDT: 2.8L; protocol-based standard care: 3.3L; usual-care: 2.3L (P<.001) 2- dobutamine use: EGDT: 8.0%; protocol-based: 1.1%; usual care 0.9%, (P<0.001) 3- PRBC: EGDT: 14.4%; protocol-based: 8.3%; usual care: 7.5% (P = 0.001) 4- <b>Primary outcome:</b> 60 day mortality: EGDT: 21.0%; protocol-based: 18.2%; usual care: 18.9% (P=.55 for three way comparison) 5- No differences in other primary endpoints. 6- <b>Secondary outcomes:</b> Need for Renal replacement Therapy was higher in protocol-based standard care: protocol-based: 6.0%; EGDT: 3.1%; usual-care: 2.8% (P=0.04)								
Conclusion	1- There is no significant advantage, with respect to mortality or morbidity, of protocol-based resuscitation over bedside care that was provided according to the treating physician's judgment 2- There is no significant benefit of the mandated use of central venous catheterization and central hemodynamic monitoring in all patients								
Take Home Point	ProCESS identifies early recognition of sepsis, early administration of antibiotics, early adequate volume resuscitation, and clinical assessment of the adequacy of circulation as the elements we should focus on to save lives.								
Caveats	1- 10 years after the original EGDT Rivers study, the usual-care group has changed and has potentially integrated principles of the EGDT protocol, early recognition of sepsis, early antibiotics, lower tidal volumes, tighter blood sugar control 2- We don't know if randomization was concealed. 3- The EGDT group seemed sicker at baseline (more abdominal sepsis, lower BP, longer time to randomize) . 4- External applicability: these were all academic centers, a full research team prompting clinicians to act and follow time sensitive protocols (a study coordinator, bedside nurse and a dedicated research physician).								

