

Acute Care Update - American Journal of Hospital Medicine

 medicine2.missouri.edu/jahm/acute-care-update/

April 6, 2016

Acute Care Update – 2015

Harbaksh Sangha, M.D.

Department of Medicine, Division of Pulmonary, Critical Care, and Environmental Medicine, University of Missouri School of Medicine, Columbia, MO

Sepsis Redefined

A taskforce convened by the Society of Critical Care Medicine and the European Society of Intensive Care Medicine came up with new definitions for sepsis.¹

The spectrum of organ dysfunction in sepsis will now be defined by two terms, sepsis and septic shock.

Sepsis is now defined as life-threatening organ dysfunction caused by a dysregulated host response to infection. Organ dysfunction is initially assessed with a quick sequential organ failure assessment tool (qSOFA). The variables in this tool are respiratory rate (RR), mental status and systolic blood pressure (SBP). Two or more positive qSOFA variables (RR \geq 22, altered mentation and SBP \leq 100 mmHg) should prompt a full SOFA assessment. A SOFA score of 2 or more (assuming a baseline of zero) defines sepsis (recommended ICD-10 code – R65.20).

Septic shock is now defined as a subset of sepsis patients in whom the circulatory and cellular/metabolic abnormalities are profound enough to substantially increase the mortality. Septic shock identification now includes – persistent hypotension requiring vasopressors to maintain the mean arterial pressure (MAP) of \geq 65 mmHg and a serum lactate level of $>$ 2 mmol/L despite adequate volume resuscitation (recommended ICD-10 code – R65.21).

Early Goal Directed Therapy in Sepsis

Three trials (ProCESS,² ARISE³ and ProMiSe⁴) were published addressing the goals of therapy in sepsis. The results could be summarized as:

1. Timely source control (antibiotics) and IV fluid resuscitation⁵ remain the cornerstones of treatment of sepsis.
2. Clinical symptoms and signs of hypo-perfusion (low MAP/SBP, high heart rate, altered sensorium, oliguria, skin changes and lactic acidosis etc.) should guide IV fluid resuscitation.

3. Protocol based central venous pressure (CVP) monitoring⁵ to assess the adequacy of IV fluid resuscitation does not help.
4. Similarly, protocol based treatment with packed red blood cells (PRBC) and inotropes (dobutamine),⁵ targeting mixed venous oxygen saturation monitoring (ScvO₂), does not improve outcomes.

Transfusion Threshold in Critical Illness

Three trials addressed the effects of PRBC transfusion in sepsis,⁶ upper GI bleeding,⁷ and cardiac surgery.⁸ Restrictive transfusion strategy resulted in equal or better primary outcomes in these trials. The probability of survival in the restrictive transfusion (transfuse if hemoglobin <7) group was particularly higher in patients with GI bleeding with cirrhosis and Child–Pugh class A or B disease.

Choice of IV Fluids in Sepsis

In septic patients, supplementing the crystalloids with 20% albumin (to keep the serum albumin concentration above 3 mg/dl) did not have a positive effect on the primary outcome of mortality.⁹ Based on the evidence so far,⁹⁻¹¹ crystalloids are the choice of fluids for resuscitation in sepsis.

Choice of Crystalloids in Critical Illness

Normal saline remains the choice of fluids for resuscitation in sepsis. Hyperchloremia has been postulated to cause acidosis and reduction in renal blood flow.¹²⁻¹⁴ However, a recent study¹⁵ failed to show any renoprotective effects of bicarbonate based fluids in patients undergoing open-heart surgery and was stopped early after the interim analysis suggested possible harm.

Target Blood Pressure in Sepsis

In a recent trial, targeting a MAP of 80-85 mmHg did not confer a mortality advantage over a MAP of 65-70 mmHg.¹⁶ Clinical assessment of adequacy of perfusion should guide the selection of the target MAP for a particular patient. Arbitrary, pre-defined MAP and other targets lead to under or over-utilization of IV fluids and vasopressors and put patients at risk of organ damage and arrhythmias. Norepinephrine remains the vasopressor of choice,¹⁷ with adequate fluid resuscitation being the primary intervention.

Clot Retrieval in Stroke

Multiple recent trials showed that the endovascular thrombectomy with the use of a stent retriever combined with intravenous thrombolysis were more effective (improved neurologic function on modified Rankin scale) in stroke patients with proximal intracranial arterial occlusion, as compared to intravenous thrombolysis alone.¹⁸⁻²² The numbers needed to treat (NNT) were estimated to range from 3 to 7 in these studies.²³ Up to 10% of all stroke patients within 6 hours of stroke onset would qualify for this intervention.²³

Therapeutic Hypothermia following Cardiac Arrest

Despite a substantial risk of bias and lack of firm evidence for benefit²⁴ in the existing literature, the practice of therapeutic hypothermia following cardiac arrest found its way into major international guidelines and became the standard of care.²⁵ A recent, better quality trial showed no difference in the primary outcome of mortality and the secondary outcome of poor neurological outcome or death when target temperatures of 33°C and 36°C were compared.²⁶

Reversal Agents for Newer Oral Anticoagulants

Two trials came out recently, demonstrating the efficacy of the newly introduced reversal agents for oral direct thrombin inhibitor (dabigatran) and direct factor Xa inhibitors (apixaban and rivaroxaban). Idarucizumab was shown to result in complete reversal of anti-coagulant effects of dabigatran within minutes in patients with serious bleeding or requiring urgent surgery,²⁷ and andexanet reversed the anti-coagulant effects of apixaban and rivaroxaban in older healthy subjects.²⁸ Safety concerns with newer oral anticoagulants persist, especially in the elderly and in those with renal impairment.²⁹⁻³¹

Risk of Contrast Induced Nephropathy

A retrospective study involving 6902 patients with chronic kidney disease found that intravenous contrast administration was not associated with acute kidney injury, emergent dialysis or short-term mortality.³² This study comes at a time when physicians are increasingly questioning the perceived risk of contrast induced nephropathy,³³ and will go a long way in assuring physicians that IV contrast use in imaging and procedures is safe.

Diagnosis of Pulmonary Embolism

Over-diagnosis of pulmonary embolism (PE) on CT angiography has been a matter of concern for some time now. When the pretest clinical probability of PE is low, the chances of false positivity go up (42% in one study).³⁴ This concern was addressed in a recent study,³⁵ where experts in chest radiology retrospectively reviewed the positive CTA studies in a tertiary care center. 46.2% of the studies with single vessel PE were deemed discordant or negative for PE. Hence, the use of Wells criteria and d-dimer is highly recommended to select patients with higher clinical probability of PE for CTA testing.

References

1. Singer M, Deutschman CS, Seymour CW, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016;315:801-10.
2. Pro CI, Yealy DM, Kellum JA, et al. A randomized trial of protocol-based care for early septic shock. *N Engl J Med*. 2014;370:1683-93.
3. Investigators A, Group ACT, Peake SL, et al. Goal-directed resuscitation for patients with early septic shock. *N Engl J Med*. 2014;371:1496-506.
4. Mouncey PR, Osborn TM, Power GS, et al. Trial of early, goal-directed resuscitation for septic shock. *N Engl J Med*. 2015;372:1301-11.
5. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001;345:1368-77.

6. Holst LB, Haase N, Wetterslev J, et al. Lower versus higher hemoglobin threshold for transfusion in septic shock. *N Engl J Med*. 2014;371:1381-91.
7. Villanueva C, Colomo A, Bosch A, et al. Transfusion strategies for acute upper gastrointestinal bleeding. *N Engl J Med*. 2013;368:11-21.
8. Murphy GJ, Pike K, Rogers CA, et al. Liberal or restrictive transfusion after cardiac surgery. *N Engl J Med*. 2015;372:997-1008.
9. Caironi P, Tognoni G, Masson S, et al. Albumin replacement in patients with severe sepsis or septic shock. *N Engl J Med*. 2014;370:1412-21.
10. Myburgh JA, Finfer S, Bellomo R, et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. *N Engl J Med*. 2012;367:1901-11.
11. Finfer S, Bellomo R, Boyce N, et al. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *N Engl J Med*. 2004;350:2247-56.
12. Wilcox CS. Regulation of renal blood flow by plasma chloride. *J Clin Invest*. 1983;71:726-35.
13. Chowdhury AH, Cox EF, Francis ST, Lobo DN. A randomized, controlled, double-blind crossover study on the effects of 2-L infusions of 0.9% saline and plasma-lyte(R) 148 on renal blood flow velocity and renal cortical tissue perfusion in healthy volunteers. *Ann Surg*. 2012;256:18-24.
14. Aksu U, Bezemer R, Yavuz B, Kandil A, Demirci C, Ince C. Balanced vs unbalanced crystalloid resuscitation in a near-fatal model of hemorrhagic shock and the effects on renal oxygenation, oxidative stress, and inflammation. *Resuscitation*. 2012;83:767-73.
15. Haase M, Haase-Fielitz A, Plass M, et al. Prophylactic perioperative sodium bicarbonate to prevent acute kidney injury following open heart surgery: a multicenter double-blinded randomized controlled trial. *PLoS Med*. 2013;10:e1001426.
16. Asfar P, Meziani F, Hamel JF, et al. High versus low blood-pressure target in patients with septic shock. *N Engl J Med*. 2014;370:1583-93.
17. De Backer D, Biston P, Devriendt J, et al. Comparison of dopamine and norepinephrine in the treatment of shock. *N Engl J Med*. 2010;362:779-89.
18. Berkhemer OA, Fransen PS, Beumer D, et al. A randomized trial of intraarterial treatment for acute ischemic stroke. *N Engl J Med*. 2015;372:11-20.
19. Goyal M, Demchuk AM, Menon BK, et al. Randomized assessment of rapid endovascular treatment of ischemic stroke. *N Engl J Med*. 2015;372:1019-30.
20. Campbell BC, Mitchell PJ, Kleinig TJ, et al. Endovascular therapy for ischemic stroke with perfusion-imaging selection. *N Engl J Med*. 2015;372:1009-18.
21. Saver JL, Goyal M, Bonafe A, et al. Stent-retriever thrombectomy after intravenous t-PA vs. t-PA alone in stroke. *N Engl J Med*. 2015;372:2285-95.
22. Jovin TG, Chamorro A, Cobo E, et al. Thrombectomy within 8 hours after symptom onset in ischemic stroke. *N Engl J Med*. 2015;372:2296-306.
23. Furlan AJ. Endovascular therapy for stroke—it's about time. *N Engl J Med*. 2015;372:2347-9.
24. Nielsen N, Friberg H, Gluud C, Herlitz J, Wetterslev J. Hypothermia after cardiac arrest should be further evaluated—a systematic review of randomised trials with meta-analysis and trial sequential analysis. *Int J Cardiol*. 2011;151:333-41.

25. Scirica BM. Therapeutic hypothermia after cardiac arrest. *Circulation*. 2013;127:244-50.
26. Nielsen N, Wetterslev J, Cronberg T, et al. Targeted temperature management at 33 degrees C versus 36 degrees C after cardiac arrest. *N Engl J Med*. 2013;369:2197-206.
27. Pollack CV, Jr., Reilly PA, Eikelboom J, et al. Idarucizumab for Dabigatran Reversal. *N Engl J Med*. 2015;373:511-20.
28. Siegal DM, Curnutte JT, Connolly SJ, et al. Andexanet Alfa for the Reversal of Factor Xa Inhibitor Activity. *N Engl J Med*. 2015;373:2413-24.
29. Legrand M, Mateo J, Aribaud A, et al. The use of dabigatran in elderly patients. *Arch Intern Med*. 2011;171:1285-6.
30. Maddry JK, Amir MK, Sessions D, Heard K. Fatal dabigatran toxicity secondary to acute renal failure. *Am J Emerg Med*. 2013;31:462 e1-2.
31. Lillo-Le Louet A, Wolf M, Soufir L, et al. Life-threatening bleeding in four patients with an unusual excessive response to dabigatran: implications for emergency surgery and resuscitation. *Thromb Haemost*. 2012;108:583-5.
32. McDonald JS, McDonald RJ, Lieske JC, et al. Risk of Acute Kidney Injury, Dialysis, and Mortality in Patients With Chronic Kidney Disease After Intravenous Contrast Material Exposure. *Mayo Clin Proc*. 2015;90:1046-53.
33. Katzberg RW, Lamba R. Contrast-induced nephropathy after intravenous administration: fact or fiction? *Radiol Clin North Am*. 2009;47:789-800.
34. Stein PD, Fowler SE, Goodman LR, et al. Multidetector computed tomography for acute pulmonary embolism. *N Engl J Med*. 2006;354:2317-27.
35. Hutchinson BD, Navin P, Marom EM, Truong MT, Bruzzi JF. Overdiagnosis of Pulmonary Embolism by Pulmonary CT Angiography. *Am J Roentgenol*. 2015;205:271-7.