

**Washington University Emergency Medicine Journal Club**  
**Balanced Fluid Resuscitation**

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### Vignette

It's another busy day TCC, when an elderly female rolls in from triage with fever, cough, and a new oxygen requirement. Her vitals are T 38.3 BP 90/42 , HR 115, RR 24, SpO2 88% on RA. Even before you see the patient you are concerned for pneumonia with severe sepsis. You institute early antibiotics, fluids, serial lactates and systematically begin to aggressively resuscitate her. The patient requires nearly five liters of normal saline before her blood pressure stabilizes. Proud of your resuscitation, you tweet out #crushingsepsis and #normalsaline4life which gets an immediate response from Dr. Evan Schwarz, who happened to be trolling your twitter feed. He tweets "More like #increasedrenalfailure and #trybalancedfluids". Inspired by his tweets you perform a brief literature review on the topic of 'balanced fluid' resuscitation.

#### PICO Question

**Population:** Critically ill adult patients (e.g. patients with severe sepsis or septic shock)

**Intervention:** Balanced fluids (e.g. lactated ringers)

**Comparison:** Chloride rich fluids (e.g. normal saline)

**Outcome:** Mortality, renal failure, need for renal replacement therapy, cost, length of stay

### Search Strategy

No formal search strategy was used. Articles were chosen by Drs. Louis Jamtgaard and Evan Schwarz, in part based on research done for a [recent article by Dr. Schwarz in EPMonthly](#).

**Article 1:** [Raghunathan K, Shaw A, Nathanson B, Stürmer T, Brookhart A, Stefan MS, Setoguchi S, Beadles C, Lindenauer PK. Association between the choice of IV crystalloid and in-hospital mortality among critically ill adults with sepsis. Crit Care Med. 2014 Jul;42\(7\):1585-91. \[Answer Key\]\(#\).](#)

**Article 2:** [Raghunathan K, Bonavia A, Nathanson BH, Beadles CA, Shaw AD, Brookhart MA, Miller TE, Lindenauer PK. Association between Initial Fluid Choice and Subsequent In-hospital Mortality during the Resuscitation of Adults with Septic Shock. Anesthesiology. 2015 Sep 28. \[Answer Key\]\(#\).](#)

**Article 3:** [Yunos NM, Bellomo R, Hegarty C, Story D, Ho L, Bailey M. Association between a chloride-liberal vs chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. JAMA. 2012 Oct 17;308\(15\):1566-72. \[Answer Key\]\(#\).](#)

**Article 4:** [Young P, Bailey M, Beasley R, Henderson S, Mackle D, McArthur C, McGuinness S, Mehrrens J, Myburgh J, Psirides A, Reddy S, Bellomo R; SPLIT Investigators; ANZICS CTG. Effect of a Buffered Crystalloid Solution vs Saline on Acute Kidney Injury Among Patients in the Intensive Care Unit: The SPLIT Randomized Clinical Trial. JAMA. 2015 Oct 27;314\(16\):1701-10. \[Answer Key\]\(#\).](#)

### Bottom Line

Normal saline has long been the “go to” fluid of choice for resuscitation in the ED for critically ill patients. However, the use of such “chloride rich” or “unbalanced” fluids has been controversial for decades, with many calling for the use of fluids that more closely resemble the tonicity of human blood. For example, aggressive resuscitation with isotonic saline has been shown to decrease serum pH, without affecting serum osmolality ([Williams 1999](#)), and has been suggested to increase the risk of renal dysfunction ([Lobo 2014](#)). The clinical significance of these and similar effects has been called into question over the last decade. We sought to evaluate the evidence for and against the use of balanced fluid resuscitation in ED patients, particularly those with severe sepsis or septic shock.

Unfortunately, no articles addressing fluid choice in emergency department patients were identified. All four articles were conducted in the ICU, making it difficult to generalize the results to our patient population. This is especially true in two of the papers: in one of these only 22% of patients were admitted from the ED, half were post-operative, and nearly a third were admitted following elective surgery ([Yunos 2012](#)); in the other, patients were noted to be primarily post-operative, and the majority of these were following elective surgery ([Young 2015](#)). Neither of these studies demonstrated a reduction in acute kidney injury (AKI), need for renal replacement therapy, or mortality with the use of balanced fluids. While both studies were prospective, and the study by Yunos et al was randomized, the patients were overall less sick than patients traditionally admitted to the ICU from the ED, making it difficult to apply these results to our patient population ([external validity](#)).

Two less methodologically robust, retrospective studies were identified, that at least included patients more similar to those in our setting ([Rhagunathan 2014](#), [Rhagunathan 2015](#)). These two studies were conducted using the same retrospective cohort of patients from 360 US ICUs with sepsis requiring vasopressor therapy. Unfortunately, as these were retrospective studies, the two treatment groups were unbalanced, and statistical methods had to be employed to balance the two cohorts. In the first of these studies, patients receiving any amount of balanced fluid were [propensity matched](#) to patients receiving only unbalanced fluids during the same time period. Patients who received some balanced fluids saw a decrease in in-hospital mortality (RR 0.86, 95% CI 0.78-0.94; NNT 31) with no difference in AKI or need for dialysis. A dose-response relationship was also observed, in which the relative risk of in-hospital mortality was lowered an additional 3.4% on average for every 10% increase in the proportion of balanced fluids received. In the second study, multiple methods were used to adjust for baseline differences between groups, including propensity matching, [inverse probability weighting](#), and [logistic](#)

[regression](#). Regardless of the method used, the use of balanced fluids was associated with a decrease in in-hospital mortality.

Unfortunately, there are no prospective, randomized trials in ED patients assessing the efficacy of balanced fluids in resuscitation. While there are theoretical benefits, none of these has yet been proven. The current data consists of a fairly methodologically sound, randomized trial and a before and after study, each conducted with a relatively healthy cohort of patients that seem quite disparate from critically ill patients in the ED, and two retrospective observational trials of septic ICU patients in which patients were treated at clinician discretion. While these two latter trials utilized statistical methods to attempt to balance known confounders between the groups, these methods do not replace randomization when evaluating their methodological rigor. The current evidence is fair at best, but with varying outcomes, making it difficult to provide a clear recommendation. Further prospective studies should be conducted using critically ill ED patients, in order to help us make better decisions regarding our fluid administration options, particularly in those patients undergoing large-volume resuscitation. Given the relatively few downsides to balanced fluid administration, it seems reasonable to opt for lactated ringer's or Hartmann's solution when administered a large volume of fluid to patient, particularly when such a patient may already be acidotic.