



Which crystalloid should we be using for the resuscitation of septic patients?

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Article type: Systematic Review and Meta-Analysis

Ratings: *Methods*—2.5, *Usefulness*—3.5

were used to evaluate bias. Publication bias was assessed with funnel plot and Egger's regression analysis.

Primary outcomes

1. Mortality.
2. Acute kidney injury.

Secondary outcomes

1. Renal replacement therapy.
2. ICU length of stay.

Introduction

Sepsis and septic shock are very common emergency department presentations. Fluid resuscitation with crystalloids along with early antibiotic administration are currently cornerstones of sepsis management [2]. The authors sought to evaluate the impact of normal saline as compared with balanced crystalloids in the resuscitation of septic patients.

Methods

The authors completed a systematic review of three databases for cohort and randomized controlled studies that compared balanced crystalloids to normal saline in patients with sepsis. A random-effects meta-analysis was completed. Jadad and the Newcastle Ottawa Quality Assessment Scale

Main results

The authors screened 355 unique citations and found 15 studies which met their inclusion criteria. They included 8 RCT and 7 retrospective cohort studies from United States (6), Asia (4), Europe (2), Australasia (2), and South America (1) with a total 20, 329 patients

Outcomes (number of studies)	RR (95% CI)	p-value
Mortality (15)	0.88 (0.81 – 0.96)	0.005
Acute Kidney injury (7)	0.85 (0.77 – 0.93)	0.0006
Renal replacement therapy (6)	0.91 (0.76 – 1.08)	0.28

Primary and secondary outcomes across all studies

Outcomes (number of studies)	RR (95% CI)	p-value
Mortality (8)	0.92 (0.82 – 1.02)	0.11
Acute Kidney Injury (2)	0.71 (0.47 – 1.06)	0.09
Renal Replacement Therapy (2)	0.71 (0.36 – 1.41)	0.33

Primary and secondary outcomes across RCTs only

There was no significant difference in ICU length of stay (median duration – 0.25 days (95% CI – 3.44 TO 2.95 days, $p = 0.88$). This result was reported in 3 cohort studies, 0 RCTs.

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Appraisal

Strengths

- Exhaustive search strategy, with no restriction on language or country.
- Search terms reported and reproducible.
- Adherent to PRISMA guidelines.
- Sub-group analyses decided a priori.
- Sub-group analyses performed based on enrollment location (ED vs ICU).

Limitations

- Pooling of RCT data with cohort study data warrants caution; particularly when RCT only data were not found to be statistically significant.
- Trial was not registered on PROSPERO.
- Jadad, not Cochrane risk-of-bias tool was used.

Context

The 2021 Surviving Sepsis campaign made a weak recommendation for balanced crystalloids over normal saline in the resuscitation of septic patients [2]. This recommendation was largely based on a pre-planned sub-group analysis from the SMART trial. This study compiles existing data, and adds data from two recent, large, multi-center RCTs—the BaSICS and PLUS trial—to the pool of what is currently understood about the impact of crystalloid resuscitation of septic patients.

This study also highlights the high degree of uncertainty that currently exists on this topic and supports the need for clarification in the form of either: (1) a large multi-center

RCT evaluating the impact of different crystalloids specifically in septic patients or (2) an individual patient data meta-analysis of the existing RCT data on this topic.

In the view of our local intensivist colleagues, balanced crystalloids have increasingly become the resuscitative fluid of choice for sepsis—this study provides further, albeit weak, evidence to support this practice.

Bottom line

The authors found a reduction in mortality and acute kidney injury with the use of balanced crystalloids, although these results were not statistically significant when only RCT data were analyzed.

Given the low risk of harm and real possibility of benefit, we should resuscitate our septic patients with balanced crystalloids until we have further evidence to guide us.

Declarations

Conflicts of interest The authors have no conflicts of interest to declare.

References

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2. Evans L, Rhodes A, Alhazzani W, Antonelli M, Coopersmith CM, French C, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021. *Crit Care Med.* 2021;49(11):e1063–143.