

Effect of restrictive versus liberal fluid management strategies on major adverse kidney events in critically ill adult patients: Protocol for systematic review and meta-analysis

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Introduction

Importance of Fluid Therapy in Critical Care

Given to improve cardiac output or restore vital signs (1,2).

There is a lack of agreement on the appropriate amount of fluid to administer in the critically ill

Benefits of restrictive fluid management (3-7):

- decreased mortality
- improved renal function
- shorter hospital & ICU length of stay
- Reduced need for organ support (e.g., mechanical ventilation)
- Limitations** of previous meta-analyses:
 - Lack of generalizability due to focus on subpopulations
 - Low quality (e.g., other than RCT) included studies
 - Lack of consistent definitions of fluid balance

Gap in the Literature:

- Current studies have mainly focused on critically ill subpopulations (i.e., sepsis or acute respiratory distress syndrome).
- The influence of fluid restriction on patient outcomes for all critically ill patients has yet to be studied

Clinical Significance

Our rigorous review analyzes outcome data on fluid restriction for all ICU patients with a focus on high quality evidence

Objectives

To understand the effects of lower cumulative fluid exposure (restrictive fluid therapy) versus higher cumulative fluid exposure (liberal fluid therapy) on patient outcomes, especially major adverse kidney events (MAKE) in ICU adults.

Primary Outcome: MAKE by 30 days- composite outcome of death, new RRT, or persistent renal dysfunction (9).

Secondary Outcomes: MAKE at 60 and 90 days; and mortality, new RRT, and persistent renal dysfunction at 30,60, and 90 days.

Methodology

Search Strategy

Search strategy was created with support from medical librarians at the SHA (MD, LM)

Databases searched between May - June 2021: Ovid MEDLINE, PubMed, EMBASE, CINAHL, Web of Science, the Cochrane Library, and a manual search of bibliographies from included articles.

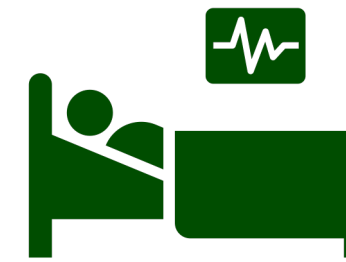
Medical subject headings (MeSH): "diuresis", "critical illness", "critical care", "intensive care units", "intensive care", "critically ill patient".

Data Selection and Extraction

Four researchers completed study selection & data extraction independently and in duplicate, using Rayyan to screen studies (8) and Microsoft Excel version 16.22 for data extraction.

Inclusion Criteria

- Randomised Controlled Trials (RCTs)**
- Any language
- Over 18 years old
- ICU population
- Fluid administration in ICU was primary focus



Statistical Analysis

Dichotomous outcomes: DerSimonian & Laird random effects meta-analysis model using an inverse-variance method to estimate the pooled RR and 95% CI (10).

Continuous outcomes: Random effects meta-analysis model using an inverse-variance method to estimate the standardized mean difference and 95% CI. We estimated statistical heterogeneity with the I^2 statistic.

Quality of studies was assessed with the Cochrane collaboration risk of bias tool (11).

Certainty of evidence was assessed with GRADE(12).

Results

Initial screen: 10,152 studies.

Full text screen: 150 studies.

Final analysis: 12 studies.

Table 1. Meta-analysis of major adverse kidney events in critically ill patients

Outcome	Studies (N)	Persons (n)	Measure of effect	95% CI	I^2	p-value	GRADE certainty assessment
30-day mortality	4	480	0.83RR	0.46-1.48	0%	0.52	Very low
90-day mortality	4	1220	0.96RR	0.58-1.60	37%	0.89	Very low
New RRT	6	2079	0.82OR	0.56-1.21	22%	0.33	Low
New AKI	5	1149	0.87RR	0.75-1.02	0%	0.09	Low

Study	Risk of bias domains					Overall
	D1	D2	D3	D4	D5	
Chen et al 2015	+	+	+	+	+	+
Corl et al 2019	+	-	+	+	+	-
Haase et al 2013	+	+	+	+	-	-
Hjortrup et al 2016	-	X	+	+	+	X
Lavu et al 2014	X	-	+	+	+	X
Parke et al 2015	+	+	+	+	+	+
Parke et al 2021	+	+	+	+	+	+
Piljic et al 2015	+	-	+	+	+	-
Semler et al 2020	-	+	+	+	+	-
Vaara et al 2021	-	X	+	+	+	X
Wiedemann et al 2006	+	-	+	+	+	-

Figure 1. Risk of bias analysis for included studies in the systematic review & meta-analysis

Conclusion

Fluid restriction did not seem to impact major adverse kidney events in critically ill patients

Compared to usual care, fluid restriction was not associated with differences in renal outcomes, length of stay, duration of mechanical ventilation, or mortality at 30, 60, or 90 days.

Limitations of our findings

The results of our study are limited by the quality of available evidence, including the small number of patients within the included studies and lack of uniform reporting across studies.

Overall, the quality of the RCTs was low, due to the concerns around bias, as well as the GRADE certainty assessment, showing a low level of confidence in the evidence.

The findings of our review indicates further, large randomized controlled trials in ICU to assess the impact of fluid management on renal outcomes

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