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THE RELATIONSHIP BETWEEN FLUID BALANCE AND FLUID MANAGEMENT STRATEGIES WITH MORTALITY AND CLINICAL OUTCOMES IN ICU: A SYSTEMATIC REVIEW

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ABSTRACT

Background : Fluid balance is one of the fundamental management aspects in critically ill patients treated in the intensive care unit (ICU). Fluid resuscitation is necessary to maintain tissue perfusion and increase cardiac output. However, excessive fluid accumulation can cause adverse effects. Several studies have shown that positive cumulative fluid balance in the early stages of ICU admission can worsen outcomes in critically ill patients and is associated with high mortality.

Methods : A literature search was conducted in the PubMed, ScienceDirect, and SpringeLink databases. Of the 834 articles, five systematic reviews and meta-analyses that assessed the relationship between fluid balance and fluid management strategies with mortality and clinical outcomes in ICU patients in the last five years and met the established inclusion and exclusion criteria were analyzed in this systematic review.

Result : Based on the search results, five systematic reviews and meta-analyses were found that were relevant to the research objective, namely the relationship between fluid balance and fluid management strategies with mortality and clinical outcomes in ICU patients. Two observational meta-analyses reported that fluid overload and positive cumulative fluid balance in the early ICU phase were consistently associated with increased short- and long-term mortality, as well as organ complications including acute kidney injury (AKI), the need for renal replacement therapy (RRT), and worsening respiratory function. Conversely, three RCT meta-analyses showed that restrictive fluid resuscitation strategies did not significantly reduce mortality but were safe to use and provided secondary benefits in the form of reduced mechanical ventilation duration.

Conclusion : Fluid overload after the resuscitation phase in the ICU is consistently associated with increased mortality and organ complications. Meanwhile, restrictive fluid strategies in clinical trials do not reduce mortality but are safe and beneficial for secondary outcomes such as mechanical ventilation duration. An individualized and phase-based fluid approach, in line with the ROSE concept, is needed to prevent fluid overload and improve outcomes in critically ill patients.

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1. Introduction

Fluid balance is one of the fundamental management aspects in critically ill patients treated in the intensive care unit (ICU), where fluid balance often changes in critical illness. Fluid resuscitation is necessary to maintain tissue perfusion and increase cardiac output. However, excessive fluid accumulation can cause adverse effects, including prolonged tissue edema, impaired oxygen transport, reduced metabolite diffusion, and impaired cell-cell interactions.[1]

Several studies have shown that positive cumulative fluid balance (CFB) in the early stages of ICU admission can worsen outcomes in critically ill patients and is associated with high mortality, especially in patients with acute kidney injury (AKI). A higher percentage of fluid excess is associated with increased mortality and shorter VFD (Ventilator Free Days).[1,2] Although fluid balance plays an important role in the management of critically ill patients, there is still uncertainty regarding the optimal strategy to be implemented in the ICU. Fluid Accumulation Syndrome (FAS) is known to have serious impacts on mortality, duration of mechanical ventilation, kidney function, and length of ICU stay, making the prevention of FAS as important as its treatment.[3] This systematic review aims to synthesize the latest evidence on the association between fluid balance, fluid management strategies, and clinical outcomes among adult ICU patients.

2. Methods

This systematic review was prepared based on the 2020 PRISMA guidelines to assess the relationship between fluid balance and fluid management strategies with mortality and clinical outcomes in ICU patients. Data sources were derived from article searches in PubMed, ScienceDirect, and SpringerLink using a combination of keywords ("Fluid Balance" OR "Fluid Management" OR "Fluid Overload") AND ("Intensive Care Unit" OR 'ICU' OR "Critically Ill") AND ("Treatment Outcome" OR "Mortality" OR "Clinical Outcome" OR "Prognosis"). Inclusion criteria were established using the PICOTS framework, covering systematic review/meta-analysis studies on adult ICU patients published between 2020 and 2025, in English, and with full-text access. Irrelevant studies were excluded. From 834 identified articles, after screening and eligibility, 5 suitable studies were obtained. Data extraction was performed by assessing the title, abstract, and full text. The risk of bias in observational studies was evaluated using the Newcastle Ottawa Scale (NOS), while RCT trials used the Cochrane RoB 2. Analysis was performed using the systematic literature review method to identify, evaluate, and synthesize relevant findings. The study results were then presented in the form of a qualitative synthesis, with a primary focus on mortality and clinical outcomes of ICU patients.

3. Results

Several meta-analyses have evaluated the relationship between fluid balance and clinical outcomes in critically ill patients in the ICU. In a meta-analysis by Messmer et al. (2020) involving 31 observational studies and 3 RCTs with a total of 31,076 patients, it was found that fluid overload (FO) and positive cumulative fluid balance (CFB) were closely associated with increased mortality. FO after three days of ICU care increased the risk of death nearly ninefold (RR 8.83; 95% CI 4.03–19.33), while positive CFB in the first three days was associated with a twofold increase in mortality risk (RR 2.15; 95% CI 1.51–3.07). Per-liter analysis showed that each additional liter of CFB increased mortality by 19% (RR 1.19; 95% CI 1.11–1.28). The authors concluded that both FO and positive CFB are strong predictors of mortality, especially in patients with sepsis, acute kidney injury, and post-surgery.[4]

These findings are reinforced by a recent meta-analysis by Lubis et al. (2025) that pooled 34 observational studies with a total of 49,467 critically ill patients. The results of the analysis showed that FO ≥10% was associated with an increase in 30-day mortality (RR 1.47; 95% CI 1.06–1.89). Additionally, positive CFB within the first 72 hours increased the risk of death (RR 1.29; 95% CI 1.14–1.44) and was also significantly associated with 90-day mortality (RR 1.91; 95% CI 1.49–2.32). Similar to previous studies, mortality increased with fluid accumulation, with a 16% increase in risk for each additional liter of CFB (RR 1.16; 95% CI 1.01–1.33). The authors emphasized the importance of early fluid control to mitigate the adverse effects of fluid overload.[5]

The meta-analysis by Reynolds et al. (2023) reviewed eight RCT studies with a total of 2,375 sepsis patients to assess the impact of restrictive resuscitation strategies. The results showed no significant difference in mortality compared to standard care (RR 0.90; 95% CI 0.76–1.06). However, the restrictive strategy provided benefits in secondary outcomes, namely a reduction in the duration of mechanical ventilation by approximately 1.25 days (95% CI -1.92 to -0.58). Thus, fluid restriction after the initial resuscitation phase was not proven to reduce mortality, but it was beneficial in accelerating respiratory recovery.[6]

Furthermore, a meta-analysis by Duan et al. (2025) involving five RCTs with 1,972 patients with septic shock also found similar results. The restrictive strategy did not show a significant advantage over the conventional approach in terms of ICU mortality (RR 1.00; 95% CI 0.90–1.12), AKI incidence (RR 0.92; 95% CI 0.79–1.07), or mechanical ventilation requirements (RR 0.96; 95% CI 0.74–1.23). The authors concluded that although not superior, restrictive fluid resuscitation remains safe and can be considered as an alternative fluid therapy strategy in patients with septic shock.[7]

Consistent findings were also reported by Shahnoor et al. (2023), who conducted a meta-analysis of 12 RCTs in patients with sepsis and septic shock. The results showed that the restrictive strategy was not associated with a reduction in mortality (RR 0.98; 95% CI 0.90–1.05), but significantly reduced the duration of mechanical ventilation (MD -1.02 days; 95% CI -1.65 to -0.38). No significant differences were found in ICU length of stay, AKI incidence, or need for renal replacement therapy. The authors emphasize that restrictive resuscitation is safe to use and provides respiratory benefits despite not affecting mortality rates.[8]

Overall, meta-analysis evidence indicates that fluid overload and positive cumulative fluid balance consistently increase mortality risk in ICU patients, particularly from large-scale observational studies. Meanwhile, restrictive fluid resuscitation strategies in RCTs have not been proven to reduce mortality, but they provide other clinical benefits such as shortening the duration of mechanical ventilation. This underscores the importance of an adaptive, individualized fluid approach tailored to the phase of the disease, with the aim of preventing excessive fluid accumulation that adversely affects both short-term and long-term outcomes.

4. Discussion

This systematic review analyzes five articles in the form of systematic reviews and meta-analyses that assess the relationship between fluid balance and mortality and clinical outcomes in ICU patients. Two observational meta-analyses (Messmer et al., 2020; Lubis et al., 2025) consistently show that positive fluid balance (CFB positive) and fluid overload (FO) are closely associated with increased mortality. Messmer reported that each 1-liter increase in CFB increases the risk of death by 19%, while Lubis emphasized that FO ≥5% or positive CFB in the first 72 hours increases short- and long-term mortality. These results emphasize that fluid accumulation after the initial resuscitation phase is a strong predictor of poor clinical outcomes.

Conversely, three meta-analyses based on randomized controlled trials (Reynolds et al., 2023; Duan et al., 2025; Shahnoor et al., 2023) evaluated restrictive fluid resuscitation strategies compared to conventional fluid therapy in patients with sepsis or septic shock. All three reported that fluid restriction did not significantly reduce mortality. However, restrictive strategies still showed several other benefits: Reynolds and Shahnoor noted a shorter duration of mechanical ventilation, while Duan reported that this strategy did not increase the risk of AKI, the need for RRT, or ischemic events, so it can be considered safe in clinical practice.

Positive FO/CFB has a major impact on mortality, especially in patients with acute kidney injury (AKI). The mechanisms involved include increased intra-abdominal pressure, which reduces renal perfusion, and renal venous congestion, which impairs venous return and exacerbates kidney injury. In patients with acute lung injury, positive CFB is associated with further oxygenation impairment and longer mechanical ventilation requirements. Some studies even report that negative fluid balance is associated with lower short-term mortality.[9]

In patients with acute lung injury, positive fluid balance is associated with further oxygenation impairment and longer mechanical ventilation requirements. On the other hand, negative fluid balance has been recommended as an indication for early discontinuation of mechanical ventilation. Several observational studies have reported that negative fluid balance is associated with lower risk-adjusted short-term mortality compared to patients with positive fluid balance.[10]

In patients with heart failure, fluid management is more complex. In the early phase, fluid administration may be needed to increase cardiac output, but patients are then prone to fluid overload. This indicates that fluid strategies must be tailored to the phase of the disease and the patient's hemodynamic status.[11]

Fluid management in the ICU can be guided by the ROSE model (Resuscitation, Optimization, Stabilization, Evacuation). In the resuscitation phase, positive fluid balance is still needed to restore tissue perfusion. However, in the optimization and stabilization phases, fluid targets should be neutral or slightly negative. Furthermore, during the evacuation (deresuscitation) phase, the focus shifts to reducing fluid excess through spontaneous diuresis, diuretic administration, or renal replacement therapy (CRRT). Observational evidence suggests that positive CFB within the first 72 hours in the ICU is associated with increased mortality, making daily fluid balance evaluation crucial.[12,13]

Overall, strong observational evidence supports that positive FO/CFB is an important risk factor for mortality and other poor outcomes in critically ill patients. However, RCTs evaluating restrictive strategies have not demonstrated a reduction in mortality, despite other benefits such as reduced duration of mechanical ventilation. This indicates that fluid management cannot be standardized but must be adaptive to the patient's disease phase.

5. Conclusion

Five meta-analyses show that fluid overload (FO) and positive cumulative fluid balance (CFB) after initial resuscitation are closely associated with increased mortality and organ complications, particularly renal failure and respiratory disorders, in ICU patients. Meanwhile, restrictive fluid strategies have been proven to be safe and capable of shortening the duration of mechanical ventilation, although they have not been consistently shown to reduce mortality rates. These findings emphasize the need for individualized fluid management based on the disease phase using the ROSE approach (Resuscitation, Optimization, Stabilization, Evacuation/de-resuscitation). With the appropriate strategy, fluid overload can be prevented, organ complications reduced, ICU

length of stay shortened, and short- and long-term clinical outcomes improved, although stronger evidence from randomized clinical trials is still needed.

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