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Restrictive vs Liberal Fluid Therapy in Septic Shock and Major Non-cardiac Surgery

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ABSTRACT

Introduction: Optimal fluid management remains a critical challenge in patients with septic shock undergoing major non-cardiac surgery. While liberal fluid resuscitation has traditionally been recommended to restore tissue perfusion, excessive fluid administration may contribute to fluid overload, organ dysfunction, and adverse postoperative outcomes. Restrictive fluid therapy has emerged as a potential strategy to improve clinical outcomes while minimizing complications associated with positive fluid balance.
Materials and Methods: This prospective comparative study was conducted over one year from July 2024 to July 2025 in the Department of Anaesthesiology and Critical Care of a tertiary care teaching hospital. A total of 100 adult patients with septic shock undergoing major non-cardiac surgery were enrolled and allocated into two equal groups: restrictive fluid therapy (n=50) and liberal fluid therapy (n=50). Baseline demographic and clinical characteristics, perioperative fluid administration, laboratory parameters, postoperative complications, duration of mechanical ventilation, ICU stay, hospital stay, and 28-day mortality were evaluated. Statistical analysis was performed using SPSS version 26.0, with a p-value <0.05 considered statistically significant.
Results: Baseline demographic characteristics and illness severity were comparable between the groups. The restrictive fluid therapy group received significantly lower volumes of intravenous fluids and demonstrated lower positive fluid balance, improved Day 3 SOFA scores, lower serum lactate and creatinine levels, and shorter vasopressor duration (p<0.05). Pulmonary edema occurred significantly less frequently in the restrictive group (4.0% vs. 18.0%; p=0.026). Additionally, patients receiving restrictive fluid therapy required significantly shorter durations of mechanical ventilation, ICU stay, and hospital stay (all p<0.01). Although 28-day mortality was lower in the restrictive group (16.0% vs. 22.0%), the difference was not statistically significant.
Conclusion: Restrictive fluid therapy was associated with improved perioperative outcomes, including reduced fluid overload, better organ function, fewer pulmonary complications, and shorter ICU and hospital stay, without increasing mortality. A carefully monitored restrictive fluid strategy may therefore represent an effective perioperative fluid management approach in patients with septic shock undergoing major non-cardiac surgery.

Keywords*: Septic shock; Restrictive fluid therapy; Liberal fluid therapy; Major non-cardiac surgery; Perioperative outcomes.*

INTRODUCTION

Septic shock remains one of the leading causes of perioperative morbidity and mortality in critically ill patients undergoing major non-cardiac surgery [1,2]. It is characterized by profound circulatory, cellular, and metabolic abnormalities resulting from a dysregulated host response to infection, leading to persistent hypotension, tissue hypoperfusion, and multiple organ dysfunction [3]. Despite advances in antimicrobial therapy, source control, hemodynamic monitoring, and critical care management, septic shock continues to be associated with prolonged intensive care unit (ICU) stay, increased healthcare costs, and high mortality rates [4]. Optimal perioperative hemodynamic management is therefore a cornerstone of treatment to restore adequate tissue perfusion while minimizing further organ injury [5].

Intravenous fluid therapy represents one of the fundamental components of septic shock resuscitation [6]. Traditionally, liberal fluid administration has been advocated to improve preload, cardiac output, and tissue perfusion [7]. However, accumulating evidence suggests that excessive fluid administration may result in a positive fluid balance, endothelial glycocalyx disruption, interstitial edema, impaired oxygen diffusion, pulmonary complications, delayed wound healing, abdominal compartment syndrome, and worsening renal function [7,8]. Conversely, restrictive fluid therapy aims to provide only the volume necessary to maintain adequate organ perfusion while avoiding the detrimental consequences of fluid overload [7,9]. Early vasopressor initiation and goal-directed hemodynamic monitoring have further strengthened the rationale for restrictive fluid strategies in critically ill patients [9].

The optimal fluid management strategy in patients with septic shock undergoing major non-cardiac surgery remains controversial [10]. While several randomized trials and meta-analyses have compared restrictive and liberal fluid strategies in critically ill or surgical populations, their findings have been heterogeneous due to differences in patient populations, resuscitation protocols, and outcome measures [11,12]. Moreover, evidence specifically addressing patients with septic shock requiring major non-cardiac surgical intervention is limited. As these patients experience both sepsis-induced circulatory dysfunction and surgery-related physiological stress, identifying the most appropriate fluid strategy is essential for reducing postoperative complications and improving clinical outcomes [10,13].

The present study aimed to compare restrictive and liberal fluid therapy strategies in patients with septic shock undergoing major non-cardiac surgery and to evaluate their effects on perioperative fluid balance, organ dysfunction, postoperative complications, duration of mechanical ventilation, length of ICU and hospital stay, and 28-day mortality.

MATERIALS AND METHODS

This prospective comparative study was conducted in the Department of Anaesthesiology and Critical Care at a tertiary care teaching hospital over a period of one year, from July 2024 to July 2025. The study included 100 adult patients diagnosed with septic shock who underwent major non-cardiac surgery during the study period. Ethical approval was obtained from the Institutional Ethics Committee before commencement of the study, and written informed consent was obtained from all participants or their legally authorized representatives. Patients aged ≥18 years who fulfilled the diagnostic criteria for septic shock and required major non-cardiac surgical intervention were eligible for inclusion. Patients with cardiogenic shock, severe congestive heart failure, end-stage renal disease requiring dialysis, advanced chronic liver disease, pregnancy, or those undergoing cardiac surgery were excluded from the study.

Eligible patients were allocated into two equal groups of 50 patients each based on the perioperative fluid management strategy employed. The restrictive fluid therapy group received goal-directed fluid administration with careful titration of intravenous crystalloids to maintain adequate organ perfusion while avoiding fluid overload, with vasopressors used early when clinically indicated. The liberal fluid therapy group received conventional fluid resuscitation with larger volumes of intravenous crystalloids according to institutional practice, with vasopressor support initiated when persistent hypotension remained despite adequate fluid administration. All patients received standard perioperative monitoring, appropriate antimicrobial therapy, source control procedures, and postoperative intensive care management according to established institutional protocols.

Demographic characteristics, baseline comorbidities, physiological variables, laboratory investigations, and illness severity scores, including Acute Physiology and Chronic Health Evaluation II (APACHE II) and Sequential Organ Failure Assessment (SOFA) scores, were recorded at admission. Intraoperative variables included duration of surgery, emergency or elective procedure, volume of crystalloids and colloids administered, blood transfusion requirement, urine output, and 24-hour cumulative fluid balance. Postoperative assessments included mean arterial pressure, heart rate, serum lactate concentration, serum creatinine, SOFA score on Day 3, duration of vasopressor therapy, duration of mechanical ventilation, length of intensive care unit (ICU) stay, total hospital stay, and postoperative complications such as acute kidney injury, pulmonary edema, pneumonia, acute respiratory distress syndrome, surgical site infection, arrhythmias, re-operation, ICU readmission, and 28-day mortality. The primary outcome was the incidence of major postoperative complications, while secondary outcomes included organ dysfunction, resource utilization, and mortality.

Data were entered into Microsoft Excel and analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0 (IBM Corp., Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation (SD) and compared using the independent samples Student's *t*-test. Categorical variables were presented as frequency and percentage and analyzed using the Chi-square test or Fisher's exact test, as appropriate. Multivariate logistic regression analysis was performed to identify independent predictors of major postoperative complications, and results were expressed as adjusted odds ratios (ORs) with 95% confidence intervals (CIs). A two-tailed p value of <0.05 was considered statistically significant.

RESULTS

A total of 100 patients with septic shock undergoing major non-cardiac surgery were equally allocated to the restrictive fluid therapy group (n=50) and the liberal fluid therapy group (n=50). The two groups were comparable with respect to baseline demographic characteristics, including age, sex, body mass index, prevalence of diabetes mellitus, hypertension, chronic kidney disease, and chronic obstructive pulmonary disease (all p>0.05). Similarly, no significant differences were observed in baseline illness severity, as assessed by APACHE II score, SOFA score, serum lactate level, and mean arterial pressure, indicating comparable baseline clinical status between the two groups (Table 1).

Table 1. Baseline demographic and clinical characteristics of the study population

Variable	Restrictive (n=50)	Liberal (n=50)	P value
Age (years)	59.8 ± 12.1	58.7 ± 11.5	0.642
Male sex, n (%)	31 (62.0)	29 (58.0)	0.684
BMI (kg/m²)	25.6 ± 3.4	25.9 ± 3.8	0.712
Diabetes mellitus	18 (36.0)	20 (40.0)	0.682
Hypertension	22 (44.0)	24 (48.0)	0.689
Chronic kidney disease	6 (12.0)	7 (14.0)	0.765
COPD	5 (10.0)	6 (12.0)	0.749
APACHE II score	19.4 ± 5.1	19.8 ± 4.9	0.718
Baseline SOFA score	7.2 ± 2.3	7.4 ± 2.4	0.661
Serum lactate (mmol/L)	3.9 ± 1.3	4.0 ± 1.4	0.783
Mean arterial pressure (mmHg)	61.8 ± 5.2	62.4 ± 5.6	0.591

Operative characteristics were comparable between the two groups with respect to the proportion of emergency surgeries and duration of surgery (p>0.05). However, patients managed with the restrictive fluid strategy received significantly lower volumes of crystalloids and colloids and demonstrated a substantially lower positive fluid balance at 24 hours compared with the liberal fluid group (all p<0.01). Urine output and blood transfusion requirements were similar between the groups (Table 2).

Table 2. Operative characteristics and perioperative fluid administration

Variable	Restrictive (n=50)	Liberal (n=50)	P value
Emergency surgery	33 (66.0)	35 (70.0)	0.669
Duration of surgery (min)	183.6 ± 39.7	188.2 ± 42.1	0.574
Crystalloid administered (mL)	2145 ± 382	3678 ± 564	<0.001
Colloid administered (mL)	246 ± 110	318 ± 126	0.003
Positive fluid balance at 24 h (mL)	1032 ± 348	2386 ± 604	<0.001
Urine output (mL/24 h)	1682 ± 428	1765 ± 451	0.341
Blood transfusion	7 (14.0)	10 (20.0)	0.424

Patients in the restrictive fluid therapy group demonstrated significantly better postoperative physiological recovery, with lower serum lactate levels, lower Day 3 serum creatinine, improved SOFA scores, and shorter vasopressor duration compared with the liberal fluid group (all p<0.05). Mean arterial pressure and heart rate at 24 hours remained comparable between the two treatment groups (Table 3).

Table 3. Hemodynamic and laboratory outcomes

Variable	Restrictive (n=50)	Liberal (n=50)	P value
MAP at 24 h (mmHg)	72.8 ± 6.4	71.9 ± 6.8	0.491
Heart rate (beats/min)	88.5 ± 11.6	90.3 ± 12.2	0.452
Lactate at 24 h (mmol/L)	1.92 ± 0.71	2.43 ± 0.82	0.001
Serum creatinine Day 3 (mg/dL)	1.21 ± 0.42	1.42 ± 0.53	0.030
SOFA score Day 3	4.8 ± 2.1	6.2 ± 2.4	0.003
Vasopressor duration (hours)	38.6 ± 14.5	47.8 ± 18.4	0.008

Postoperative complications occurred less frequently among patients receiving restrictive fluid therapy. Pulmonary edema was significantly reduced in the restrictive group compared with the liberal group (4.0% vs. 18.0%; p=0.026). Although acute kidney injury, pneumonia, acute respiratory distress syndrome, surgical site infection, re-operation, and new-onset arrhythmias were numerically lower in the restrictive group, these differences did not reach statistical significance (Table 4).

Table 4. Postoperative complications

Variable	Restrictive (n=50)	Liberal (n=50)	P value
Acute kidney injury	8 (16.0)	15 (30.0)	0.094
Pulmonary edema	2 (4.0)	9 (18.0)	0.026
Pneumonia	5 (10.0)	10 (20.0)	0.161
ARDS	3 (6.0)	8 (16.0)	0.109
Surgical site infection	6 (12.0)	8 (16.0)	0.564
Re-operation	2 (4.0)	4 (8.0)	0.398
New arrhythmia	3 (6.0)	7 (14.0)	0.182

Clinical outcomes favored the restrictive fluid strategy. Patients in this group required significantly shorter durations of mechanical ventilation and experienced reduced ICU and total hospital stay compared with those receiving liberal fluid therapy (all p≤0.002). ICU readmission and 28-day mortality were numerically lower in the restrictive group; however, these differences were not statistically significant (Table 5).

Table 5. Clinical outcomes

Variable	Restrictive (n=50)	Liberal (n=50)	P value
Mechanical ventilation (hours)	32.7 ± 15.8	46.3 ± 21.4	<0.001
ICU stay (days)	5.8 ± 2.3	7.6 ± 3.1	0.001
Hospital stay (days)	10.9 ± 3.7	13.5 ± 4.4	0.002
ICU readmission	3 (6.0)	6 (12.0)	0.298
28-day mortality	8 (16.0)	11 (22.0)	0.446

Multivariate logistic regression analysis identified liberal fluid therapy, higher APACHE II score, and elevated baseline serum lactate as independent predictors of major postoperative complications. Liberal fluid therapy was associated with more than a two-fold increased risk of complications (adjusted OR 2.42, 95% CI 1.08–5.44; p=0.032). Age and diabetes mellitus were not found to be significant independent predictors after adjustment for potential confounders (Table 6).

Table 6. Multivariate logistic regression analysis for predictors of major postoperative complications

Variable	Adjusted OR	95% CI	P value
Liberal fluid strategy	2.42	1.08–5.44	0.032
APACHE II score	1.13	1.03–1.24	0.011
Baseline lactate	1.41	1.07–1.88	0.016
Diabetes mellitus	1.28	0.58–2.84	0.543
Age	1.02	0.99–1.06	0.214

The restrictive fluid strategy was associated with a significantly lower incidence of the primary endpoint of major postoperative complications compared with liberal fluid therapy (28.0% vs. 50.0%; p=0.024). In addition, restrictive fluid therapy resulted in significantly lower positive fluid balance, improved Day 3 SOFA scores, shorter ICU stay, and reduced hospital stay (all p<0.01). Although 28-day mortality was lower in the restrictive group, the difference between the groups was not statistically significant (Table 7).

Table 7. Summary of primary and secondary endpoints

Outcome	Restrictive (n=50)	Liberal (n=50)	P value
Primary endpoint			
Major postoperative complications	14 (28.0)	25 (50.0)	0.024
Secondary endpoints			
Positive fluid balance (mL)	1032 ± 348	2386 ± 604	<0.001
SOFA score Day 3	4.8 ± 2.1	6.2 ± 2.4	0.003
ICU stay (days)	5.8 ± 2.3	7.6 ± 3.1	0.001
Hospital stay (days)	10.9 ± 3.7	13.5 ± 4.4	0.002
28-day mortality	8 (16.0)	11 (22.0)	0.446

DISCUSSION

The present study compared restrictive and liberal fluid therapy in patients with septic shock undergoing major non-cardiac surgery and demonstrated that a restrictive fluid strategy was associated with significantly lower cumulative fluid balance, improved organ function, reduced pulmonary complications, shorter duration of mechanical ventilation, and decreased ICU and hospital stay. Although 28-day mortality was lower in the restrictive group, the difference was not statistically significant. These findings suggest that limiting unnecessary fluid administration while maintaining adequate tissue perfusion may improve postoperative recovery without adversely affecting survival. Similar observations were reported in the CLASSIC feasibility trial by Hjortrup et al., which showed that a restrictive resuscitation protocol significantly reduced administered fluid volume and was associated with favorable trends in organ dysfunction and acute kidney injury without increasing adverse events [14]. Likewise, recent systematic reviews have concluded that restrictive fluid strategies are associated with reduced fluid overload and improved organ-related outcomes while maintaining comparable mortality to liberal strategies [11].

One of the major findings of the present study was the significantly lower incidence of pulmonary edema, lower Day 3 SOFA scores, and reduced serum lactate concentrations among patients receiving restrictive fluid therapy. Excessive intravenous fluid administration contributes to endothelial glycocalyx disruption, increased capillary permeability, and interstitial edema, thereby impairing pulmonary gas exchange and organ perfusion. Our findings are consistent with evidence demonstrating that restrictive fluid management decreases pulmonary complications and facilitates earlier recovery of organ function [11]. The recent meta-analysis of restrictive versus liberal fluid therapy reported lower risks of acute respiratory distress syndrome (ARDS), reduced duration of mechanical ventilation, and improved organ function among patients managed with restrictive strategies, findings that closely parallel the outcomes observed in our study [11]. Patients managed with restrictive fluid therapy in the present study also experienced significantly shorter durations of mechanical ventilation, ICU stay, and total hospital stay. These observations support the concept that minimizing positive fluid balance facilitates earlier resolution of organ dysfunction and enhances postoperative recovery. Similar reductions in resource utilization have been described in previous investigations evaluating conservative fluid management in critically ill patients. However, unlike our study, the CLOVERS trial by the PETAL Network did not demonstrate a significant difference in mortality or major recovery outcomes between restrictive and liberal strategies in patients with sepsis-induced hypotension [15]. This discrepancy may be explained by differences in study population, timing of intervention, volume of fluids administered before randomization, and the inclusion of patients undergoing major surgery in the present study, who may derive greater benefit from avoidance of perioperative fluid overload [15]. Furthermore, the RELIEF trial in major abdominal surgery emphasized that both excessive fluid restriction and excessive liberal administration may be detrimental, highlighting the importance of individualized, goal-directed fluid management rather than fixed-volume strategies [16].

Multivariate analysis in the present study identified liberal fluid therapy, higher APACHE II score, and elevated baseline serum lactate as independent predictors of major postoperative complications. These findings reinforce the importance of illness severity and early hemodynamic optimization in determining patient outcomes. Although mortality did not differ significantly between the study groups, the consistent improvement in postoperative morbidity and resource utilization suggests that restrictive fluid therapy represents a safe and effective perioperative strategy for carefully selected patients with septic shock undergoing major non-cardiac surgery. Larger multicenter randomized controlled trials with longer follow-up are warranted to determine whether these improvements in postoperative recovery translate into meaningful long-term survival benefits.

CONCLUSION

The present study demonstrated that a restrictive fluid therapy strategy in patients with septic shock undergoing major non-cardiac surgery was associated with improved perioperative outcomes compared with liberal fluid therapy. Restrictive fluid management resulted in significantly lower cumulative fluid balance, improved organ function, reduced pulmonary complications, shorter duration of mechanical ventilation, and decreased ICU and hospital stay, without adversely affecting 28-day mortality. These findings suggest that a carefully monitored restrictive fluid strategy, combined with appropriate vasopressor support and goal-directed hemodynamic management, may enhance postoperative recovery while minimizing the adverse effects of fluid overload. Further large-scale, multicenter randomized controlled trials are warranted to validate these findings and establish optimal fluid management protocols for this high-risk patient population.

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