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Impact of late fluid balance on clinical outcomes in the critically ill surgical and trauma population☆

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ABSTRACT

Purpose: Management of fluid status in critically ill patients poses a significant challenge due to limited literature. This study aimed to determine the impact of late fluid balance management after initial adequate fluid resuscitation on in-hospital mortality for critically ill surgical and trauma patients.
Materials and Methods: This single-center retrospective cohort study included 197 patients who underwent surgical procedure within 24 hours of surgical intensive care unit admission. Patients with high fluid balance on postoperative day 7 (>5 L) were compared with those with a low fluid balance (≤5 L) with a primary end point of in-hospital mortality. Subgroup analyses were performed based on diuretic administration, diuretic response, and type of surgery.
Results: High fluid balance was associated with significantly higher in-hospital mortality (30.2 vs 3%, $P < .001$) compared with low fluid balance; this relationship remained after multivariable regression analysis. High fluid balance was associated with increased mortality, independent of diuretic administration, diuretic response, and type of surgery.
Conclusions: Consistent with previous literature, high fluid balance on postoperative day 7 was associated with increased in-hospital mortality. Patients who received and responded to diuretic therapy did not demonstrate improved clinical outcomes, which questions their use in the postoperative period.

1. Introduction

Management of fluid status continues to be challenging in the critically ill patient. Adequate initial fluid resuscitation is essential to avoid an imbalance in systemic oxygen delivery and oxygen demand, which can result in hypoperfusion and subsequent shock. However, emerging data suggest that positive fluid balance is associated with poor clinical outcomes including prolonged duration of mechanical ventilation, intensive care unit (ICU) and hospital length of stay, anastamotic leak, and increased mortality [1–6]. Although the mechanism behind the association with poor clinical outcomes is unknown, aggressive, large-volume resuscitation may increase pulmonary edema, decrease lung compliance, and increase workload for respiration [7,8].

In surgical and trauma patient populations, there is limited evidence on effects of positive fluid balance in both the initial resuscitative period and the immediate period after this acute phase [9–13]. Excessive initial fluid administration in trauma patients is proposed to increase risk for worsened hemorrhage due to potential dislodgement of clots and dilutional coagulopathy [9]. Poor clinical outcomes, including increased mortality and intraoperative blood loss, acute lung injury, compartment syndrome, and prolonged duration of mechanical ventilation, have been observed in both penetrating and blunt trauma patients receiving aggressive initial fluid resuscitation [9–13]. Most of these trials, however, were conducted in the prehospital setting and may not directly apply to management of trauma patients in the emergency department or after hospital admission.

Currently, there is inadequate literature to guide fluid balance management after the acute resuscitative period in the critically ill trauma and surgical populations. Although available literature does suggest that positive fluid balance is associated with worse clinical outcomes, most studies have focused on septic and acute lung injury patients. The few published studies assessing fluid balance in the surgical and trauma populations suggest a similar negative influence of liberal fluid strategies on clinical outcomes, including increased rates of pneumonia, pulmonary edema, hospital length of stay, and postoperative complications [14,15]. However, these studies are limited to the immediate postoperative period and primarily reflect initial resuscitation rather than postoperative management. The objective of this study is to determine the impact of late (postoperative day [POD] 7) fluid balance after adequate initial fluid resuscitation on in-hospital mortality for critically ill surgical and trauma patients. It was hypothesized that patients with high fluid balance in the late postoperative period have worse clinical outcomes compared with those with low fluid balance.

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2. Materials and methods

2.1. Patient population

Mechanically ventilated patients aged 18 to 89 years admitted to the surgical ICU (SICU) between November 1, 2011, and October 1, 2013, who underwent a surgical procedure within 24 hours before or after SICU admission were eligible for evaluation. Patients were required to have adequate initial fluid resuscitation, defined as urine output of at least 0.5 mL kg^{-1} h^{-1} for the initial 12-hour postoperative period, to be included. To primarily assess patients requiring more aggressive fluid resuscitation, patients admitted by the following services were included: trauma, acute care surgery, colorectal surgery, gastrointestinal surgery, bariatric surgery, gynecologic oncology, surgical oncology, thoracic surgery, orthopedic surgery, plastic surgery, and transplant surgery. Exclusion criteria included incarceration, pregnancy, SICU length of stay less than 7 days, or admission to any of the following services: neurosurgery, neurovascular, burn, otolaryngology, peripheral vascular surgery, oral maxillofacial surgery, or postpartum obstetrics. Although patients on the burn service require aggressive fluid administration, they were excluded from this analysis due to the use of a colloid-based resuscitation protocol at our institution. For patients who underwent multiple surgical procedures, data collection was performed starting on POD 1 from the initial procedure occurring within 24 hours of SICU admission. During the study period, there was no specific protocol or criteria for fluid or diuretic administration in the SICU. Determination of intravascular fluid balance and initiation of therapy (fluid vs vasopressor vs diuretic) was based on continuous analysis by the ICU multidisciplinary team. Goal-directed fluid administration is provider specific with clinical decisions largely based on urine output and blood pressure, with use of lactate, central venous pressure (CVP), stroke volume, cardiac output, and other assessments of fluid status dependent on provider preference.

2.2. Study design

A single-center retrospective cohort study was conducted at a large academic, level 1 trauma center, to assess the impact of late fluid status on in-hospital mortality in surgical and trauma patients after obtaining approval from The Ohio State University Institutional Review Board. Patients with low fluid balance on POD 7 were compared with those with high fluid balance with a primary end point of in-hospital mortality. For the purposes of this study, low fluid balance was defined a priori as a net balance of positive 5 L or less positive on POD 7, whereas high fluid balance was used to describe patients with greater than 5 L net balance on POD 7 to account for estimated insensible losses in this critically ill population [16]. This cutoff was estimated based on an average 70-kg patient (10 mL kg^{-1} d^{-1}) which would equate to approximately 5 L at POD 7. Secondary end points include duration of mechanical ventilation, SICU and hospital length of stay, and SICU and total hospital cost. Subgroup analyses were determined a priori and were performed for patients undergoing abdominal surgery and for those receiving diuretics within the 7-day postoperative period. The patient populations selected for subgroup analysis were determined based on typical characteristics of the abdominal surgery patient population and anticipated benefit of assessing these subgroups in answering our study question. Response to diuretic was defined as an increase in urine output of 50% or greater compared with the day prior to diuretic administration. In addition, survivors of hospital admission were compared with nonsurvivors based on daily fluid balance and cumulative fluid balance.

Data were collected retrospectively from the electronic medical record, including baseline characteristics (age, sex, comorbidities to calculate the Charlson Comorbidity Index score, primary service, Simplified Acute Physiology Score [SAPS] II score, baseline calculated glomerular filtration rate, and serum creatinine), number of days hospitalized prior to SICU admission, surgical procedure(s) and whether emergent vs elective operation, administration of any diuretic or vasopressor through POD 7, and lactate, CVP, and cardiac output as available during 24 hours before or after SICU admission. Total hospital and SICU costs were obtained from the institutional finance department. Assessment of fluid balance was based on all recorded intake (including bolus and maintenance fluids, enteral and parenteral nutrition, and blood products) and output (including urine, stool, blood, and drain/tube output) while the patient was admitted to the SICU. Fluid status prior to transfer into the SICU, if applicable, was not included for purposes of analysis.

2.3. Statistical analysis

Patient characteristics were reported separately by late fluid balance status on POD 7 using mean and SD or median and interquartile range for continuous variables and frequency and percentages for categorical variables. The groups were compared using t tests or Wilcoxon rank sum tests for continuous variables and χ^2 or Fisher exact tests for categorical variables, as appropriate. The primary hypothesis was tested using a multivariable logistic regression model, fit to the dichotomous outcome in-hospital mortality. Low vs high fluid balance on POD 7 was the primary independent variable. The model included covariates adjusting for age, sex, SAPS II (less age component), Charlson Comorbidity Index, and abdominal surgery vs other surgery [17,18]. Age was removed from the SAPS II score in the model as age was included as a separate covariate.

Secondary analyses included investigation of the primary hypothesis within subgroups based on type of surgery (abdominal or other) and administration of a diuretic within the 7-day postoperative period. The secondary outcomes of total duration of mechanical ventilation, SICU and hospital length of stay, and total hospital and SICU cost were compared between groups by linear regression models, adjusting for the same variables as the primary analysis. Duration of ventilation and both length of stay measures were right skewed and log-transformed for analysis. Logistic regression was used to compare in-hospital mortality and duration of mechanical ventilation in subgroups of abdominal surgery and other surgery and subgroups of diuretic recipients and nonrecipients. All models included the same covariates as the primary analysis, with the exception of the abdominal surgery subgroups, which no longer included a covariate for abdominal surgery. Sensitivity analyses using fewer covariates were performed for the subgroup analyses. Two models were fit for each subgroup. The first adjusted only for age and SAPSII and the second was the univariable model for low vs high fluid balance. Statistical tests were performed at a type I error rate of $\alpha = .05$. All analyses were performed using SAS/STAT software (SAS Institute Inc., Cary, NC), version 9.3.

3. Results

A total of 3598 patients were screened, with 101 patients meeting the inclusion criteria for the low fluid balance group and 96 patients for the high fluid balance group (Fig. 1). Primary reasons for exclusion were length of stay in SICU less than 7 days, surgical service, or no surgical procedure within 24 hours of SICU admission. Baseline characteristics were similar between the groups, although the high fluid balance group had significantly higher rates of abdominal surgery, median Charlson Comorbidity Index, and SAPS II scores (Table 1). Most patients were admitted to the SICU on their first day of hospitalization, and greater than 70% underwent emergent surgery. Upon admission to the SICU, the average lactate for all patients was greater than 3 mmol/L, with low rates of acute and chronic kidney dysfunction in both groups. Patients included in the study had a high severity of illness, evidenced by a median SAPS II score higher than 40 in both groups, equating to greater than 25% predicted mortality [18].

The primary outcome of in-hospital mortality was significantly increased in the high fluid balance group compared with the low fluid balance group (30.2% vs 3.0%, $P < .001$). In the multivariable logistic