



## Impact of positive fluid balance on critically ill surgical patients: A prospective observational study



Galinos Barmbaras, MD<sup>a</sup>, Douglas Liou, MD<sup>a</sup>, Debora Lee, BS<sup>a</sup>, Nicole Fierro, BS<sup>a</sup>, Matthew Bloom, MD<sup>a</sup>, Eric Ley, MD<sup>a</sup>, Ali Salim, MD<sup>b</sup>, Marko Bukur, MD<sup>c,d,\*</sup>

<sup>a</sup> Department of Surgery, Division of Acute Care Surgery, Cedars-Sinai Medical Center, Los Angeles, CA

<sup>b</sup> Department of Surgery, Division of Trauma, Burn, and Surgical Critical Care, Brigham and Women's Hospital, Boston, MA

<sup>c</sup> Department of Trauma and Critical Care, Delray Medical Center, Delray Beach, FL

<sup>d</sup> Broward General Medical Center, Fort Lauderdale, FL

### ARTICLE INFO

#### Keywords:

Fluid balance  
Fluid overload  
Negative fluid balance  
Mortality  
Infections

### ABSTRACT

**Purpose:** The purpose of this study is to determine the effect of postoperative fluid balance (FB) on subsequent outcomes in acute care surgery (ACS) patients admitted to the surgical intensive care unit (ICU).

**Material and methods:** Acute care surgery patients admitted to the surgical ICU from 06/2012 to 01/2013 were followed up prospectively. Patients were stratified by FB into FB-positive (+) and FB-negative (−) groups by surgical ICU day 5 or day of discharge from the surgical ICU.

**Results:** A total of 144 ACS patients met inclusion criteria. Although there was no statistically significant difference in crude mortality (11% for FB [−] vs 15.5% for FB [+];  $P = .422$ ), after adjusting for confounding factors, achieving an FB (−) status by day 5 during the surgical ICU stay was associated with an almost 70% survival benefit (adjusted odds ratio [95% confidence interval], 0.31 [0.13, 0.76];  $P = .010$ ). In addition, achieving a fluid negative status by day 1 provided a protective effect for both overall and infectious complications (adjusted odds ratio [95% confidence interval], 0.63 [0.45, 0.88];  $P = .006$  and 0.64 [0.46, 0.90];  $P = .010$ , respectively).

**Conclusions:** In a cohort of critically ill ACS patients, achieving FB (−) status early during surgical ICU admission was associated with a nearly 70% reduction in the risk for mortality.

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## 1. Introduction

The concept of goal-directed resuscitation with balanced intravenous fluid administration has been a mainstay of critical care. Earlier studies showed that achieving supranormal physiologic end points with aggressive fluid resuscitation was associated with improved survival [1,2]. However, current investigations have shown this approach to be of questionable value and, in fact, may be deleterious to patients [3,4]. Most recently, a mounting body of evidence demonstrates that intensive care unit (ICU) patients who achieve a negative fluid balance (FB) status during their ICU stay have improved outcomes with regards to morbidity and even mortality. Fluid accumulation leading to a positive FB status has been shown to be associated with increased mortality in septic patients [5,6] and in patients with acute renal failure [7]. It has also been shown to increase the duration of mechanical ventilation in patients with acute lung

injury [8], increase pulmonary complications in traumatic brain injury patients [9], and result in delay of return of bowel function in patients undergoing elective bowel resection [10]. For trauma patients in particular, aggressive early crystalloid resuscitation appears to be related to a higher risk for acute respiratory distress syndrome (ARDS) and infectious complications [11]. Administration of even relatively low volumes of crystalloids in the emergency department has been also shown to lead to increased mortality, independent of age [12]. Abdominal compartment syndrome [13] and coagulopathy [14] are well-described consequences of excessive fluid administration.

Nonetheless, to date, very little prospective evidence is available to support the correlation between judicious fluid management and outcomes in patients admitted to the surgical ICU. Most reports have included nonsurgical patients. For trauma patients, most available studies focus on the initial resuscitation period. Because of the lack of evidence, we sought to conduct a prospective observational study with the aim to characterize the importance of achieving a negative FB and its effect on outcomes in a purely surgical patient population admitted to the surgical ICU. Our hypothesis was that patients achieving and maintaining a negative FB status during their surgical ICU course have higher survival and lower risk for postoperative complications.

\* Corresponding author. Herbert Wertheim, College of Medicine, Florida International University, Associate Professor of Clinical Biomedical Science; Charles E Schmidt, College of Medicine, Florida Atlantic University, Trauma and Surgical Critical Care, Broward General Medical Center, Director of Trauma Research, Delray Medical Center. Tel.: +1 561 498 4440; fax: +1 561 495 3103.

E-mail address: [mbukur@browardhealth.org](mailto:mbukur@browardhealth.org) (M. Bukur).

## 2. Methods

The Cedars-Sinai Medical Center has a dedicated acute care surgery (ACS) service that includes 7 attending staff members supported by a level I trauma center and a 24-bed dedicated surgical ICU. The institutional review board approved the conduction of this study, and a waiver of informed consent was granted. Patients at least 18 years old admitted to the surgical ICU under the ACS service from 6/1/2012 until 12/31/2012 were followed up prospectively, and demographic and clinical data were abstracted from the charts on a daily basis by a dedicated research staff using a comprehensive collection datasheet. Data acquired included age, sex, body mass index (BMI), preadmission comorbidities including hypertension, atrial fibrillation, coronary artery disease (CAD), chronic obstructive pulmonary disease (COPD), etc, reason for admission, surgical interventions, the Acute Physiology and Chronic Health Evaluation (APACHE) IV score, admission laboratory values including lactate and pH, administration of intravenous drips including vasoactive medications and insulin, and administration of antibiotics or antifungals. In addition, the total intake (crystalloids, colloids, blood products, total parenteral nutrition, enteral feeds, drips, and other medications) and output (urine, drains, dialysis, and ostomy outputs) with their components were recorded on a daily basis for the first 5 consecutive surgical ICU days.

Enrolled patients were subsequently stratified into 2 groups based on their FB status. Patients who achieved and sustained a negative FB by day 5 or on the day of discharge from the surgical ICU, whichever occurred first, were considered FB negative (−). Patients not meeting this criterion were considered FB (+). For the FB (−) patients, the day they achieved FB-negative status, defined as the day after which they remained in FB-negative status, was also recorded.

Primary outcome was in-hospital mortality, and secondary outcomes included complications during the surgical ICU stay, ventilation days, and surgical ICU length of stay. Complications included development of ARDS [15], acute lung injury [15], gastrointestinal bleeding, arrhythmia, myocardial infarction, pleural effusion, deep venous thrombosis, pulmonary embolus, systemic inflammatory response syndrome [16], sepsis [16], ventilator-associated pneumonia (VAP) [17], catheter-related blood stream infection [17], urinary tract infection [17], wound infection [17], abscess formation [17], and bacteremia [17].

Both groups were compared using  $\chi^2$  for dichotomous variables and  $t$  test for continuous variables. Clinically relevant cut-points for continuous variables were created for the purposes of the comparison, and these included age more than 60 years, BMI more than 30, APACHE IV more than 20, admission lactate more than 7 mg/dL, and admission pH less than or equal to 7.20. Complications were grouped under 2 variables: overall complications, which included the sum of all complications encountered during the surgical ICU stay and infectious/inflammatory complications, which included systemic inflammatory response syndrome, sepsis, VAP, catheter-related blood stream infection, urinary tract infection, wound infection, abscess, and bacteremia. Differences in outcomes were examined using a logistic regression to adjust for confounding factors between the 2 groups.

An additional analysis was conducted to derive factors independently associated with mortality. For the purposes of this analysis, a Cox regression was used incorporating all available covariates, which were different between patients who died and those who survived at a  $P < .200$  level, with the FB entered into the regression as a time-dependent variable. The same process was applied to identify factors independently associated with development of overall and infectious/inflammatory complications. Statistical analyses were completed using the IBM Statistical Product and Service Solutions (SPSS) (IBM, Armonk, NY) Statistics version 20.0.

## 3. Results

During the 6-month study period, 144 patients were admitted to the surgical ICU under the ACS service. The mean  $\pm$  SD (median) age

was  $55.3 \pm 24.8$  (54.5) years, 67.4% were male, 68.8% had a traumatic injury, and 56.9% were mechanically ventilated (Table 1). Patients with the worst physiologic derangements and an admission APACHE IV score more than 20 comprised 63.6% of the study population. In addition, 21.2% of the patients were on vasoactive medications on admission (Table 1).

Overall, the study population was almost evenly divided, with 71 patients (49.3%) being FB (+) and 73 (50.7%) being FB (−). A univariate analysis showed that there were no differences between the 2 groups with regards to age, sex, BMI, APACHE IV scores, admission lactate and pH, mechanical ventilation, use of vasoactive medications, and insulin drip utilization (Table 1). However, a significantly higher proportion of FB (−) patients received antibiotics/antifungals compared with their FB (+) counterparts (60.3% vs 42.3%;  $P = .031$ ).

Most enrolled patients (63.2%) had a concomitant morbidity before their admission, and this was not different between the 2 groups (64.4% vs 62.0%;  $P = .764$ ) (Table 2). There was also no difference noted for any specific comorbidity, including hypertension, atrial fibrillation, CAD, COPD, diabetes mellitus (DM), cirrhosis, or end-stage renal disease (Table 1).

**Table 1**

Comparison of basic demographic and clinical data between patients with a positive FB FB (+) and those with a negative FB (−)

	Total (n = 144)	FB (−) <sup>a</sup> (n = 73)	FB (+) <sup>a</sup> (n = 71)	P
Age (y) mean $\pm$ SD (median)	55.3 $\pm$ 24.8 [54.5]	55.8 $\pm$ 21.3 [56.0]	54.9 $\pm$ 28.1 [52.0]	.827
Age >60 (y), %	41.5%	42.3%	40.8%	.865
Male, %	67.4%	68.5%	66.2%	.769
BMI mean $\pm$ SD (median)	26.6 $\pm$ 6.5 [25.5]	26.4 $\pm$ 6.4 [25.6]	26.8 $\pm$ 6.8 [25.1]	.778
BMI >30%	22.2%	19.2%	25.4%	.373
APACHE IV mean $\pm$ SD (median)	37.2 $\pm$ 29.2 [29.8]	37.5 $\pm$ 29.7 [32.6]	36.9 $\pm$ 29.0 [28.8]	.903
APACHE IV >20.0%	63.6%	60.0%	67.2%	.396
Lactate (mg/dL) mean $\pm$ SD (median)	2.7 $\pm$ 3.0 [2.0]	2.7 $\pm$ 3.7 [1.7]	2.7 $\pm$ 2.2 [2.2]	.950
Lactate >7 (mg/dL), %	4.6%	3.2%	5.9%	1.000
pH mean $\pm$ SD (median)	7.30 $\pm$ 0.32 [7.34]	7.25 $\pm$ 0.43 [7.32]	7.36 $\pm$ 0.09 [7.36]	.097
pH $\leq$ 7.20%	6.3%	8.0%	4.3%	.679
Mechanical ventilation, %	56.9%	58.9%	54.9%	.630
Vasoactive medications, %	21.5%	21.9%	21.1%	.908
Antibiotics/antifungals, %	51.4%	60.3%	42.3%	.031
Insulin drip, %	9.7%	8.2%	11.3%	.537
Trauma, %	68.8%	68.5%	69.0%	.946
Bowel obstruction, %	11.1%	13.7%	8.5%	.316
Cholecystitis, %	2.8%	1.4%	4.2%	.363
GI bleeding, %	7.6%	9.6%	5.6%	.372
Necrotizing soft tissue infection, %	2.8%	2.7%	2.8%	.978
Surgical intervention				
- Exploratory	27.8%	24.7%	31.0%	.397
- laparotomy, %				
- Bowel resection, %	15.3%	16.4%	14.1%	.695
Any comorbidity, %	63.2%	64.4%	62.0%	.764
- Hypertension, %	33.3%	35.6%	31.0%	.556
- Atrial fibrillation, %	11.8%	13.7%	9.9%	.475
- CAD, %	16.0%	13.7%	18.3%	.450
- COPD/emphysema, %	9.0%	6.8%	11.3%	.355
- CVA, %	1.4%	1.4%	1.4%	1.000
- DM, %	16.0%	17.8%	14.1%	.542
- Cirrhosis, %	3.5%	2.7%	4.2%	.679
- ESRD, %	3.5%	4.1%	2.8%	1.000
- Other, %	46.5%	46.6%	46.5%	.991

GI indicates gastrointestinal; CVA, cerebrovascular accident; ESRD, end-stage renal disease. P values were extracted from  $\chi^2$  and  $t$  test for categorical and continuous variables, respectively.

<sup>a</sup> On surgical ICU day 5 or on last surgical ICU day, whichever occurred first.

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