CUMULATIVE FLUID BALANCE AS A MAJOR PREDICTOR OF CLINICAL OUTCOME IN PATIENTS ADMITTED TO SURGICAL INTENSIVE CARE UNIT

Muhammad Sohaib, Madiha Hashmi, Faisal Shamim, Fazal Hameed Khan

Aga Khan university Hospital Karachi Pakistan

ABSTRACT

Objective: Fluid balance remains a highly controversial topic in the critical care field, and there is no consensus about the amount of fluid required by critically ill patients. In this study, the objective was to find the relationship between fluid balance and in hospital mortality in critically ill surgical patients. Our secondary objective was to identify the association between use of colloid and acute kidney injury and use of blood products and development of ARDS.

Study Design: The medical records of adult patients admitted to a surgical intensive care unit (ICU) >48 hours, from Aug 2014 to Feb 2016 (18 months) were reviewed retrospectively.

Place and Duration of Study: The study was conducted in the surgical intensive care unit of a tertiary care hospital. Medical records of 18 months from Aug 2014 to Feb 2016 were reviewed.

Material and Methods: Sampling technique was convenience sampling. A total of 100 patients met the inclusion criteria. Abstracted data of patients admitted to surgical intensive care included body mass index, Acute physiology and chronic health evaluation (APACHE)-II scores, fluid balance during first 5 days of ICU stay, length of ICU stay and in hospital mortality. All statistical analysis was performed using statistical packages for social science version 19 (SPSS Inc., Chicago, IL). Frequency and percentage were computed for qualitative observation and were analyze by chi-square test. Mean (±Standard deviation) and median (IQR) were presented for quantitative variables and analyze by independent sample t-test and Mann-Whitney test. Normality of quantitative data was also be checked by Kolmogorov-Smirnov test. Statistically significant results had a *p*-value less than 0.05.

Results: A total of 100 patients fulfilled the inclusion criteria. The average age of patients was 44.08 ± 18.14 (years), BMI (kg/m^2) 27.84 ± 5.56 and APACHE II Score 17.28 ± 6.96. The in hospital mortality was 26%, median length of ICU and hospital stay was 6.91 ± 4.07 and 14.74 ± 7.78 days. In non-survivors fluid balance was significantly positive on 2nd, 3rd, 4th and 5th day of SICU (*p*-value: 0.005, 0.0005 and 0.024), APACHE II score ($p<0.02$), incidence of acute kidney injury ($p<0.004$) and mechanical ventilation days were significantly more. There was association between the use of colloid and acute kidney injury ($p<0.014$). Use of blood products was significantly associated ($p<0.03$) with development of ARDS.

Conclusion: Positive fluid balance, high APACHE II score and acute kidney injury is significantly associated with hospital mortality of non-cardiac surgical ICU patients.

Keywords: Acute kidney injury, Body Mass Index, Intensive care unit, Mechanical ventilation.

INTRODUCTION

Fluid is used for resuscitation of critically ill patients in many clinical circumstances including shock, trauma and major surgery. The physiological rationale for such therapy is to maintain homeostasis by replacing overt or covert fluid losses in order to prevent organ hypo perfusion and subsequent organ dysfunction[1,2]. Accurate assessment of fluid status depends on physical examination, hemodynamic monitoring and intake-output data recorded hourly during the ICU stay. Daily assessment of fluid balance guides medical and nursing interventions aimed at achieving physiological stability in a patient[3,4]. The topic of perioperative fluid therapy have been addressed recently in many critical care studies[5-9]. Most of these studies have divided the patients into liberal vs restrictive fluid groups.

Correspondence: Dr Muhammad Sohaib, Department of Anaesthesia, Aga Khan University Hospital Karachi Pakistan
Email: m.shoaib@yahoo.com
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However the results of these studies are not comparable as different definitions are used for liberal and restrictive fluid therapy[8]. Restrictive fluid therapy during the perioperative period reduces the postoperative complications and hospital length of stay[10-12]. On the other hand liberal fluid therapy reduces the postoperative organ dys function[8]. The use of vasopressors in case of hypovolemia may lead to ischemia and organ hypo perfusion[13]. So it is quite difficult to divide patients in liberal and restrictive groups to receive optimum fluid therapy. Rivers *et al* in 2001 showed that early goal directed therapy clearly benefit the critically ill patients in terms of decreased hospital length of stay, reduced mortality and organ dysfunction[14]. So early goal directed therapy was adopted by surviving sepsis campaign. Vasopressin in septic shock trail, Arise and ProCESS trail clearly showed that positive fluid is harmful for the patients and negates the findings of early goal directed therapy[15,16]. The current trend is towards fluid optimization in critically ill patients. Recent data shows that the type, timing and amount of fluid may affect clinical outcome. For example, administration of early fluid therapy in sepsis improves survival[17], conservative vs liberal fluid therapy in patients with acute lung injury reduces the days of mechanical ventilation[17] and synthetic colloids cause acute kidney injury[18]. In addition, the accumulated positive fluid balance contributes to increased morbidity and mortality. Studies conducted to find out the impact of fluid balance on outcome and recommendations about the type of fluid (colloid or crystalloid) to be used for resuscitation, in patients admitted to surgical intensive care unit are inconclusive. During the perioperative period fluid management is the mainstay for treating surgical patients and this fluid is strongly correlated with in hospital mortality, surgical intensive care length of stay and hospital length of stay[19]. However it is an area of great controversy that how much fluid should be given in postoperative care and during surgical critical care stay of the patient[20]. No such study has been done in this region. Therefore the aim of this retrospective study was to find out the impact of fluid balance on outcome of critically ill surgical patients and find any association between the use of colloids and complications like acute kidney injury (AKI) or acute respiratory distress syndrome (ARDS). The primary objective was to assess the impact of 5-day cumulative fluid balance (ml/kg) on outcome of these patients in terms of mortality, days of mechanical ventilation, days of intensive care unit stay and length of hospital stay. The secondary objective was to find out any association between use of colloids and AKI and the development of ARDS with use of blood products.

MATERIAL AND METHODS

After approval from departmental and hospital ethics committee this retrospective observational study was conducted from August 2014 to February 2016 in surgical intensive care of a tertiary care hospital. All the patients admitted to surgical intensive care with age more than 18 years were included in the study. Sampling technique was convenience sampling. Patients discharged/died, or do-not-resuscitate orders within 48 hours of admission, repeat operation during the 5-day study period, NYHA class IV heart failure or ejection fraction on echocardiography <30%, chronic renal failure, cardiothoracic post-surgical patients, massive hemorrhage and massive transfusion, patients undergoing palliative surgery with short life expectancy and organ transplantation patients were excluded from the study. The patient's medical record numbers were taken from ICU database and then files were retrieved from hospital record section. A paper data collection form was designed to record variables. Demographic data, body weight, acute physiology and chronic health evaluation (APACHE) II score were recorded retrospectively from ICU database. Fluid intake and output in the ICU during the first 5 postoperative days were recorded from patient's flow sheet. Fluid intake include oral, feeding and intravenous intake. Fluid output consisted of urine, drainage,

bleeding, and renal replacement amounts. Use of colloids and blood components was defined separately and were included in total intravenous intake. The fluid balance was calculated by subtracting fluid output from fluid intake. All daily fluid indices such as fluid intake, output, and balance were noted during the first to fifth day of ICU admission. All values were adjusted to the initial body weight in kilograms; therefore the "fluid index" was represented as milliliters per kilogram per day (ml/kg/day). In addition, the duration of mechanical ventilation (MV), ICU length of stay (ICULOS), and postoperative hospital length of stay (H-LOS) were also recorded. Patients were divided into 2 groups (the survivors and the non-survivors) according to in-hospital mortality. Data Analysis was performed using statistical packages for social science version 19 (SPSS Inc., Chicago, IL). Age, gender, BMI, co-morbids (Hypertension, Ischemic heart disease, diabetes, asthma, and chronic obstructive disease) and complications like AKI and ARDS were target observation of the patients. Frequency and percentage were computed for qualitative observation and analyzed by chi-square test. Mean (±Standard deviation) and median (IQR) were presented for quantitative variables and analyze by independent sample t-test and mann-whitney test. Normality of quantitative data was checked by Kolmogorov-Smirnov test. Statistical significance was of *p*-value less than 0.05. The acute kidney injury network diagnostic were used to define the acute kidney injury[8] while for acute respiratory distress syndrome Berlin definition was used.

RESULTS

A total number of 100 patients fulfilled the inclusion criteria. The average age of patients was 44.08 ± 18.14 (years), 66% patients were male and 34% were female, BMI (kg/m²) 27.84 ± 5.56 and APACHE II Score 17.28 ± 6.96. Out of enrolled patients 68% were received from the operating rooms (OR) after emergency surgical procedures, 22% underwent elective surgeries and 10% of the patients were non-operative admitted to Surgical Intensive Care Unit (SICU) from surgical floor. Vasopressors were used in 19 (38%) of the patients. The patients were divided in to two groups (survivors and non survivors) according to in hospital mortality. Univariate analysis showed that APACHE II scores (*p*<0.01), acute

Table-I: Comparison of characteristics between survivor and non-survivor.

Variables		Survivor (n=74)	Non-Survivor (n=26)	*p*-value
Age (years)		42.89 ± 18.72	47.46 ± 15.82	0.27
Height (cm)		161.69 ± 6.31	161.38 ± 6.74	0.83
Weight (kg)		71.55 ± 12.28	74.62 ± 13.33	0.28
BMI (kg/m²		27.47 ± 5.13	28.91 ± 6.52	0.25
APACHE II Score		15.86 ± 6.55	21.82 ± 6.16	<0.001
Gender	Male	52 (70.3%)	14 (53.8%)	0.12
	Female	22 (29.7%)	12 (46.2%)	
Emergency		54 (73%)	14 (53.8%)	0.19
Elective		14 (18.9%)	8 (30.8%)	
Floor		6 (8.1%)	4 (15.4%)	
Colloid		16 (21.6%)	8 (30.8%)	0.34
Blood Product		28 (37.8%)	14 (53.8%)	0.15
AKI		14 (18.9%)	16 (61.5%)	<0.001
Mechanical ventilation days		4.71 ± 4.46	7.91 ± 3.71	0.001
ICU length stay		6.46 ± 4.12	8.36 ± 3.49	0.04
Hospital length stay		15.25 ± 8.31	13.09 ± 5.30	0.22

kidney injury (p<0.01), positive fluid indices at day 2 (p<0.0005), day 3 (p<0.0005), day 4 (p<0.0005) and day 5 (p<0.001) were significantly associated with in hospital mortality as shown in table-I & II. The patients were divided in two groups according to an APACHE II score of 20, meaning groups of scores either less than or greater than 20, we compared fluid indices between survivors and non survivors in each group. There was significant difference in the fluid balance in the ICU between the groups. In the high group (APACHE II ≥20), positive fluid balance was greater in the non-survivor group at day 3 (p<0.03) than the survivor group as shown in table-II. In the low group (APACHE II ≤20), positive fluid balance was greater in the non-survivor at day 3 (p<0.001) and day 4 (p<0.001) than the non-survivor. In addition the length of mechanical ventilation days was more in non survivors while the length of hospital stay was not statistically and clinically significant. Additional finding in the study was the development of acute kidney injury in patients who received colloid in their fluid resuscitation as shown in table III (p<0.014). The patients who received blood products in the form of packed cells fresh frozen plasma and platelets also significantly developed acute respiratory distress syndrome (p<0.01) than their counter parts as shown in table-IV.

Table-II: The difference in fluid indices between the survivor & non-survivor groups of APACHEII score less than 20.

Variables	Survivor (n=74)		Non-Survivor (n=26)		*p*-value
Fluid balance (mL/kg)	**n**	**Median [Q1,Q3]**	**n**	**Median [Q1,Q3]**	
1st day	74	25.26 [10.26, 40.42]	26	29.41 [13.37, 39.92]	0.47
2nd day	74	21.05 [11.46, 36.16]	26	47.857 [22.67, 78.21]	0.001
3rd day	68	13.48 [1.69, 25.12]	24	35.71 [20.57, 73.03]	0.001
4th day	58	3.42 [-8.08, 16.19]	24	44.79 [26.95, 53.67]	0.001
5th day	46	5.67 [-5.14, 20.83]	24	21.25 [4.53, 37.57]	0.001
APACHE II Score <20					
1st day	58	25.25 [10.26, 38.87]	14	32.20 [10.15, 37.22]	0.66
2nd day	58	19.38 [9.91, 26.77]	14	45.28 [11.73, 77.17]	0.013
3rd day	52	12.39 [1.57, 22.33]	12	26.96 [20.52, 76.27]	0.001
4th day	42	3.42 [-5.76, 14.59]	12	42.85 [13.45, 55.63]	0.001
5th day	32	0.92 [-6.36, 19.19]	12	22.29 [2.66, 38.74]	0.006
APACHE II Score ≥20					
1st day	16	25.67 [7.51, 57.41]	12	29.41 [28.16, 48.01]	0.852
2nd day	16	36.38 [16.43, 66.04]	12	54.46 [23.65, 81.34]	0.094
3rd day	16	22.35 [7.55, 41.63]	12	50.71 [29.92, 63.32]	0.026
4th day	16	8.37 [-12.42, 35.71]	12	44.79 [40.06, 47.81]	0.003
5th day	14	15.56 [16.95, 27.83]	12	21.25 [16.95, 27.83]	0.099

DISCUSSION

During the perioperative period fluid management is the mainstay for treating surgical patients and fluid balance strongly correlates with in hospital mortality, surgical intensive care, length of stay and hospital length of stay[21,22]. However it is an area of great controversy that how much fluid should be given in postoperative care and during surgical critical care stay of the patient[23]. Our study results clearly showed that patients with in hospital mortality have significant positive fluid balance at 2nd, 3rd, 4th and 5th day of admission in surgical intensive care than their counter parts. APACHEII score greater than 25 is associated with 50% mortality. While in most of the studies with sepsis APACHEII score of 20 is taken as cut off value[24]. We divided the enrolled patients into two groups

based on APACHEII score greater than 20 or less than 20. Non survivors in a group of APACHEII score less than 20 were having significant positive fluid balance at day 3rd, 4th and 5th, while in other group with APACHII score greater than 20 non survivors were having positive fluid balance at only day 3rd and 4th. Our study results are consistent with other studies. One of the study from developed country showed that positive cumulative fluid balance is an independent predictor of in hospital and intensive care unit mortality[25]. Another study from USA showed that achieving negative fluid balance by day 5 in critical care setting is associated with 70% survival benefit[26]. The same results were identified in one of the study done in the South Asia that mean fluid balance quartile within 72 h, was independently associated with an increase in ICU and hospital mortality[27]. The study results also showed that increase cumulative fluid balance is associated with increase mechanical ventilation days. The possible explanation of this is that positive fluid balance increases extravascular lung water and prolong mechanical ventilator days and also increases the incidence of ventilator associated pneumonia[28]. One other interesting finding in our study was the development of acute kidney injury in patients who received synthetic colloids during their stay in intensive care unit as shown in table. Much of the recent work in critical care clearly disfavour the use of gelatin as they increase the incidence of acute kidney injury in critically ill patients. Meta-analysis done showed that hyper oncotic colloid solutions per se injure the kidney and the renal effects are colloid specific[29]. The SAFE (Saline versus Albumin Fluid Evaluation) trial compared albumin with saline for fluid administration in the ICU and found no overall difference among the groups for 28-day survival, ICU or hospital length of stay, days of mechanical ventilation, or days of renal replacement therapy[30]. A recent cocharne trail concluded that resuscitation with colloids instead of crystalloid did not reduce the mortality in trauma patients with burns or after surgery[31]. Based on the current evidence it is better to avoid colloids as resuscitative fluids. The results of our study showed a correlation between the development of ARDS and blood product administration. This fact has already been established in number of studies. PP Dobesh in his study showed that transfusion of packed red blood cells, platelets or both have been associated with development of ARDS, increases number of mechanical ventilation days and increase mortality[32]. It has been shown in one of the study that patients who received more than 5 packed red blood cells developed ARDS and the risk of ARDS increases by 6% with each unit of packed red blood cell transfused[33]. ARDS is most commonly associated with the transfusion of FFP and cryoprecipitate[33]. So restrictive strategy of blood product administration is desirable in order to prevent the development of ARDS.

Table-III: Association between use of colloids and AKI.

Acute Kidney Injury	Colloid		*p*-value
	Yes	No	
Yes	12 (50%)	18 (23.7%)	0.014
No	12 (50%)	58 (76.3%)	
Total	24	76	100

Table IV: Association of acute respiratory distress syndrome with use of blood products.

Acute Respiratory Distress Syndrome	Blood Products		*p*-value
	Yes	No	
Yes	22 (52%)	12 (21%)	0.001
No	20 (48%)	46 (79%)	
Total	42	58	100

CONCLUSION

The mortality in critically ill noncardiac postsurgical patients may be importantly related to positive fluid balance. The results of our study showed that a positive balance can have negative impact on this patient population. Fluid overload should be considered cautiously.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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