Influence of Fluid Balance on Morbidity and Mortality in Critically Ill Patients With Acute Kidney Injury

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Introduction. Fluid management in critically ill patients with acute kidney injury (AKI) is controversial. Our study is aimed to evaluate the association between fluid balance and patient outcome in AKI patients admitted to intensive care unit (ICU).
Materials and Methods. This prospective study was carried out at Lilavati Hospital and Research Centre on 130 critically ill patients with AKI admitted to ICU. Mean daily fluid balance (MDFB) was measured and its correlation with clinical characteristics and outcomes was assessed.
Results. During ICU stay, 48.2% patients had a positive and 52.8% had a negative MDFB. In the patients with positive MDFB, mean ICU stay was longer and ventilation requirement, duration of ventilation, inotrope requirement, and duration of inotrope were greater as compared to the group with negative MDFB. A significantly higher mortality rate were observed in the patients with positive MDFB as compared to negative MDFB (43.5% versus 7.4%).
Conclusions. Negative fluid balance was independently associated with a significant reduction in mortality, ICU stay, ventilator requirement, and the need for renal replacement among critically ill patients with AKI.

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INTRODUCTION

Acute Kidney Injury (AKI) in the setting of intensive care unit (ICU) had been the subject of a number of publications over the last 2 to 3 decades. Fluid balance in critically ill patients at risk for or with AKI remains controversial,[1] and aggressive fluid resuscitation has been prescribed in AKI to maintain adequate renal perfusion.[2,3] This practice paradigm appears common and perhaps dominant in ICUs worldwide.[4,5]

The concept that liberal fluid administration is good for the kidney has been recently challenged.[6] Observational studies of patients with AKI have linked a positive fluid balance (FB) before or during renal replacement therapy (RRT) with increased mortality.[7,8] Most of these studies are limited to the developed countries and reports from India are scanty. With this in view, we aimed to prospectively determine the influences of fluid balance on morbidity and mortality in critically ill patients with AKI hospitalized in ICU.

MATERIALS AND METHODS

Participants

This is a prospective observational study carried out at Lilavati Hospital and Research Centre, Mumbai, between January 2009 and December 2010. A total of 130 patients diagnosed with AKI in ICU were studied prospectively. The stages of AKI were determined using the RIFLE criteria (risk, injury, failure, loss of kidney function, and end-stage kidney disease).[9] All adult patients, aged 18 years and above, with evidence of normal baseline serum creatinine, admitted with AKI as per RIFLE criteria in the ICU were prospectively enrolled in the study. The exclusion criteria chronic kidney disease as per Kidney Disease Outcome and Quality Initiative, kidney transplantation, and obstructive uropathy.

Data Collection and Measurements

All of the patients were evaluated for the etiology of AKI based on detailed history and clinical and laboratory data. All the important major chronic preexisting comorbid conditions such as respiratory, cardiovascular, liver, neurological, and gastrointestinal diseases were noted. In addition preexisting malignancy, human immunodeficiency virus infection, tuberculosis, and any immunocompromised state were documented.

The clinical parameters in the first 24 hours of admission, including heart rate, mean arterial pressure, respiratory rate, temperature, and urine output were collected. Daily FB was calculated as the difference between fluid administered (intravenous fluids, blood products, enteral fluids, and RRT replacement fluids) and fluid lost (ultrafiltrate from RRT, when applied, urine output, blood losses, enteral losses, and drain losses). A negative FB was present when fluid loss was greater than the fluid volume administered (indicated by a negative sign), and a positive FB was present when fluid removal was less than the fluid volume administered (indicated by a positive sign).

Mean daily fluid balance (MDFB) was calculated for each day during the ICU study. The laboratory parameters measured were complete blood count, blood glucose, kidney function tests, serum electrolytes, liver function tests, coagulation profile, and arterial blood gases. As a reference, we also evaluated a general severity of illness scoring system APACHE II (acute physiology and chronic health evaluation), SAPS II (simplified acute physiology score) and its probability of death based on the score. Both scores were calculated within first 6 hours of admission.

Statistical Analysis

Quantitative variables were presented by mean ± standard deviation (if data passed normality test) or median and inter-quartile range. Qualitative variables were represented in the form of frequency and percentage. Cross-tabulations between qualitative variables were assessed by the chi-square test (with continuity correction for 2 × 2 tables). Comparison between pairs of groups for quantitative variables was done by the unpaired *t* test (if data passed normality test) or the Mann Whitney test (if data failed normality test). The Kaplan Meyer survival analysis was done. *P* values less than .05 were considered significant.

RESULTS

A total of 730 patients admitted during January 2009 to December 2010 to the ICU were enrolled in this study. Nephrology consultation was sought for 230 patients. Out of these, 70 patients were excluded from study because they had underlying chronic kidney disease, 18 patients had posttransplant status, and 12 patients had obstructive nephropathy. After these exclusions, 130 patients with AKI were enrolled in the study (17.8% of the ICU patients).

The age range of the study population was 20 to 95 years with a mean age being 59.41 ± 15.4 years. Men constituted 62.3% of the patients. The distributions of the RIFLE groups are summarized in Table 1. The various clinical and laboratory parameters of the RIFLE groups are listed in Table 2.

Of the 130 patients enrolled in the study, complete fluid balance data to ICU discharge or 60 days or death within 60 days of discharge from the hospital (whichever occurred first) were analyzed. During ICU stay, 62 patients (48.2%) had a positive MDFB and 68 (52.8%) had a negative MDFB. The patients in the positive MDFB and negative MDFB groups were compared for their age, ICU stay, mean daily fluid volume, ventilation days, inotrope days, and the APACHE II and SAPII scores. The positive MDFB was 533 mL and the negative MDFB was -223.8 mL. Among the patients with a negative MDFB, 26.5% required mechanical ventilation versus 59.7% for the patients with a positive MDFB ($P < .001$; Figure 1). Among the patients with a negative MDFB, 32.4% required vasopressor therapy versus 67.7% for the patients with a positive MDFB ($P < .05$; Figure 2).

Table 1. Staging of Acute Kidney Injury by the RIFLE

RIFLE Stage	Number of Patients (%)
Risk	9 (6.9)
Injury	54 (41.5)
Failure	60 (46.2)
Loss	7 (5.4)

Table 2. Laboratory Parameters by RIFLE Stage

Parameter	Risk	Injury	Failure
Serum creatinine, mg/dL	2.75 ± 0.35	3.31 ± 0.68	3.95 ± 0.48
Serum albumin, g/dL	2.68 ± 0.75	2.45 ± 0.75	2.27 ± 0.36
Serum bicarbonate, mg/dL	18.24 ± 4.19	17.03 ± 4.13	16.45 ± 4.73
Hemoglobin, g/dL	10.46 ± 1.19	9.80 ± 1.08	9.60 ± 0.78
Serum calcium, mg/dL	9.64 ± 3.84	9.48 ± 2.78	9.20 ± 3.46
Serum phosphorus, mg/dL	4.46 ± 1.18	4.64 ± 1.24	4.72 ± 1.62

Among the patient with a negative MDFB, 5 (7.4%) died by 60 days after admission, compared with 27 (43.5%) in the positive MDFB group ($P < .05$; Figure 3). Furthermore, maximum survivors had a negative MDFB whereas nonsurvivors had a positive MDFB. On applying the Kaplan-Meyer survival analysis between the status of MDFB and day of mortality, a significant survival benefit was observed in those who were in negative MDFB ($P = .03$; Figure 4).

In the positive MDFB group, the mean ICU stay, ventilation requirement, duration of ventilation, inotrope requirement, and duration of inotrope were greater as compared to the negative MDFB group, whereas the APACHEII score, SAPII score, and the number of organs involved were higher in the negative MDFB, suggesting that negative MDFB was associated with decreased morbidity and mortality (Tables 3 and 4).

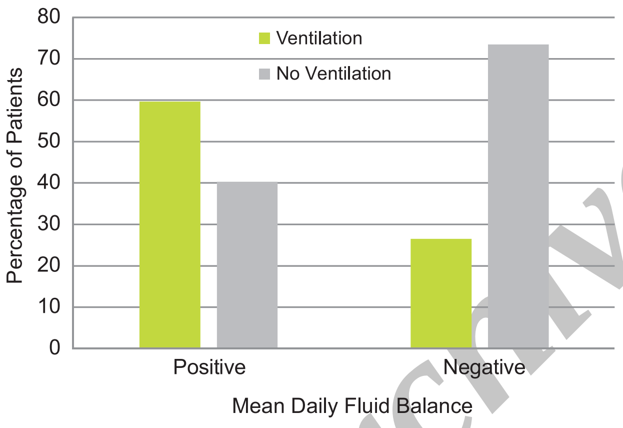

Figure 1. Association between ventilation and mean daily fluid balance

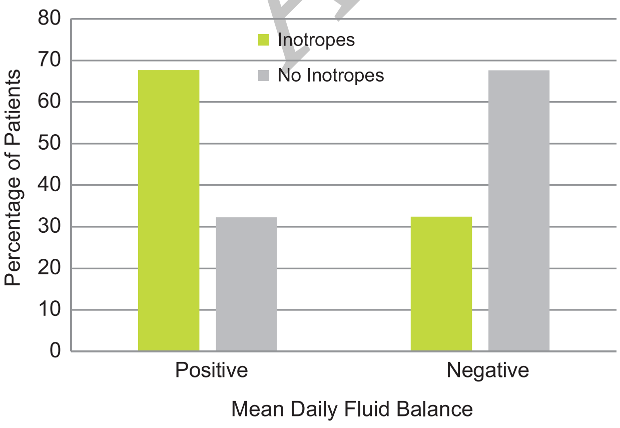

Figure 2. Association between inotropes and mean daily fluid balance

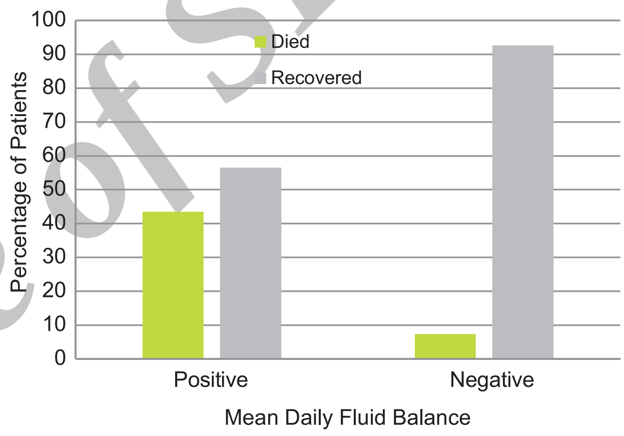

Figure 3. Association between outcome and mean daily fluid balance

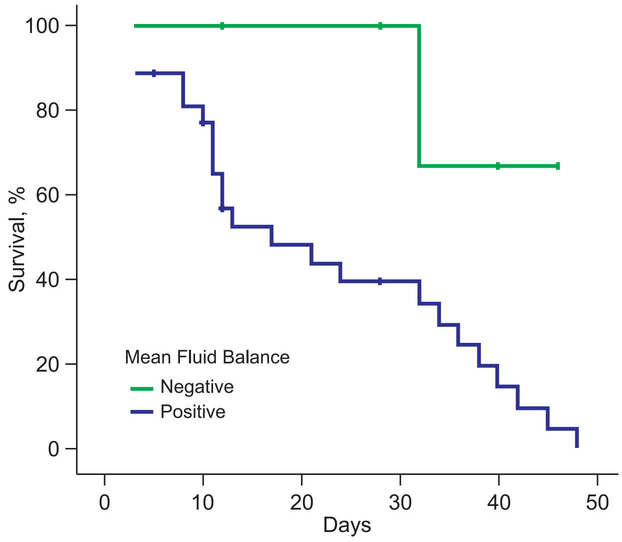

Figure 4. Kaplan-Meyer survival analysis of patients with positive versus negative mean daily fluid balance

Table 3. Characteristics of 62 Patients With Positive Mean Daily Fluid Balance

Parameter	Mean	Median (Interquartile Range)	Range
Age, y	59.58 ± 17.05	62.0 (17.8)	20 to 90
Intensive care unit stay, d	8.56 ± 5.18	7.0 (6.0)	3 to 28
Mean daily fluid balance, mL	533.00 ± 134.16	531.0 (147.8)	234 to 887
Ventilation days	2.95 ± 3.61	2.0 (5.0)	0 to 12
Number of organ involvement	1.37 ± 0.62	1.0 (1.0)	1 to 3
Inotrope days	2.85 ± 3.31	2.0 (4.0)	0 to 12
Number of inotropes	1.69 ± 1.22	2.0 (3.0)	0 to 3
FIO2	57.74 ± 14.76	60.0 (12.5)	40 to 100
Apache II	22.79 ± 7.38	22.5 (9.0)	6 to 45
SAPS II	35.62 ± 18.66	33.0 (24.0)	13 to 105

Table 4. Characteristics of 68 Patients With Negative Mean Daily Fluid Balance

Parameter	Mean	Median (Interquartile Range)	Range
Age, y	59.29 ± 16.23	65.0 (13.0)	19 to 80
Intensive care unit stay, d	5.66 ± 4.74	5.0 (3.0)	2 to 28
Mean daily fluid balance, mL	-223.79 ± 65.49	-209.5 (18.0)	-645 to -158
Ventilation days	0.93 ± 2.48	0.0 (0.0)	0 to 13
Number of organ involvement	2.32 ± 0.85	2.0 (1.0)	1 to 4
Inotrope days	0.82 ± 1.95	0.0 (1.0)	0 to 12
Number of inotropes	0.57 ± 0.92	0.0 (1.0)	0 to 3
FIO2	50.74 ± 14.46	45.0 (20.0)	25 to 100
Apache II	31.48 ± 10.39	34.0 (19.0)	15 to 55
SAPS II	52.81 ± 22.65	47.0 (30.0)	17 to 105

DISCUSSION

A relationship between a positive fluid balance and an unfavorable ICU outcome has been described before in general ICU populations. Mitchell and colleagues demonstrated a decrease in ventilator and ICU days in patients treated with fluid restriction and increased diuresis compared with a wedge pressure-guided fluid protocol.[10] Upadya and colleagues demonstrated that a negative fluid balance was independently associated with weaning success in mechanically ventilated patients.[11] In an earlier analysis of the SOAP database, Sakr and colleagues demonstrated that mean fluid balance was an independent determinant of ICU outcome in patients with acute lung injury and adult respiratory distress syndrome.[12] In patients with sepsis, the relationship between a positive fluid balance and a negative outcome has also been described. Alsous and colleagues demonstrated an increased mortality risk in patients failing to achieve a negative fluid balance within the first 3 days of treatment (relative risk, 5.0; 95% confidence interval, 2.3 to 10.9).[13] Rinaldo Bellomo et al, in the RENAL study, concluded that extra intravenous fluids may do much more harm than good. They found a negative fluid balance in ICU patients was strongly associated not only with survival and shorter ICU and hospital stays, but with a reduced need for dialysis and other RRTs.[14] Our findings are in agreement with and expand those of previous observational studies.[15-18]

Our data expand our understanding of the relationship between fluid balance and outcome. In our study, the overall mortality was 43.5 % in the positive FB group compared to 7.4 % in the negative FB group. This difference was found to be statistically significant. The consistent association between a positive FB and unfavorable outcome suggests the need to exert prudence with fluid administration in patients with AKI.[19] Another interesting finding in the present study is that outcome among patients treated with RRT was better when RRT was started early in the course of the ICU stay. Although we studied initiation of RRT in relation to ICU admission rather than to the onset of AKI as in most other studies, our results do agree with the findings of several retrospective studies that suggest that early initiation of RRT may be beneficial in AKI patients.[20-23]

Our study has several limitations. The number of studied patients is small in this study, considering high incidence of ICU admissions in the society. Another limitation of our study is the need for a baseline creatinine, which was not always available. The study was not compared with the control group (non-AKI patients).

CONCLUSIONS

Our study concludes that negative fluid balance was independently associated with a significant reduction in mortality, hospital stays, ventilator requirement, and the need for RRT among critically ill patients with AKI.

CONFLICT OF INTEREST

None declared.

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