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BIOLIFE RESEARCH ARTICLE

Fluid balance in critically ill patients, prospective observational study

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ABSTRACT

Introduction: fluid balance has recently emerged as a potential biomarker for survival in critically ill patients. Objectives: To assess the prognostic value of daily and cumulative fluid balance on mortality in the first five days for patients admitted due to critical illness. Methods: The study was conducted on 455 adult patients admitted to Critical Care Medicine Department units at Alexandria Main University Hospital with different critical diagnosis during six months from 1st January 2015 to end of June 2015. All patients were subjected on admission to complete history taking, complete physical examination, laboratory investigations, assessment of fluid intake and output as regards volume and type, APACHE II on admission and SOFA Score on 1st day of study, every 48 hours for 5 days. Results: The results revealed that for all ICU patients, negative fluid balance on any day of the study is associated with better outcomes than for patients who do not achieve negative fluid balance with regards to SOFA score, mortality, duration of mechanical ventilation and length of ICU stay. Conclusion: A positive fluid balance was strongly associated with increased mortality and other unfavorable outcomes in different subgroups of ICU patients, including longer duration of mechanical ventilation and longer ICU stay.

Keywords: Fluid balance, Critical illness, Mortality.

INTRODUCTION

Fluid therapy is a fundamental component of treatment in critically ill patients. Interestingly, fluid balance has recently emerged as a potential biomarker for survival in critically ill patients.(1)

Intravenous fluids must be used judiciously in critically ill patients as injudicious use may lead to fluid overload, pro-inflammatory reactions and may be potentially injurious. Dosing intravenous fluid during resuscitation of critically ill patients remains largely empirical. Too little fluid may result in tissue hypo-perfusion and worsen organ dysfunction, also over-prescription of fluid appears to impede oxygen delivery and compromise patient outcome.(2)

There is clear evidence suggesting that fluid overload may be detrimental in many conditions. In acute lung injury (ALI) or acute respiratory distress syndrome (ARDS), one study found that positive fluid balance was associated with worse intensive care unit (ICU) outcome, whereas other showed that conservative strategy of fluid management improved lung function and shortened the duration of mechanical ventilation and intensive care.(3-5) In severe sepsis, fluid gain was among the strongest prognostic factors for patient's mortality. It was also found that positive fluid balance (in 24, 48, and 72 hours and cumulatively from the onset of hospital admission) was associated with ventilator weaning failure.(6,7). The aim of this study is to assess the prognostic value of daily and cumulative fluid balance on mortality in the first five days for patients admitted due to critical illness.

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MATERIALS AND METHODS

Participants

This study was done in the Critical Care Medicine Department of Alexandria Main University Hospital. It was carried out 455 adult patients who are admitted to the critical care department units during six months from 1st January 2015 to end of June 2015. The study was approved by the medical ethics committee of Alexandria faculty of Medicine. An informed consent from patients' next of kin was taken before enrollment to the study.

Selection criteria:

- Patients aged 18 years and more.

Exclusion criteria:

- Patient who died within 24 hours after admission.
- Pregnant females.
- Patients admitted with burns.
- Patients admitted with cardiogenic pulmonary edema.

All patients were subjected on admission to complete history taking, complete physical examination, laboratory investigations, assessment of fluid intake and output as regards volume and type, APACHE II and SOFA Score on 1st day of study, every 48 hours for 5 days. After fulfilling the criteria, patients were resuscitated according to their different critical diagnosis and the cumulative fluid balance was assessed on the 1st, 3rd, and 5th days. Then patients were subdivided into two groups according to their cumulative balance in each of these days into the following groups;

- Positive fluid balance group.
- Negative fluid balance group0

The two groups were compared in the first 5 days according to morbidity, mortality, duration of mechanical ventilation and length of ICU stay.

Statistical Analysis:

Data were analyzed using SPSS software package version 18.0 (SPSS, Chicago, IL, USA). Quantitative data were expressed using range, mean, standard deviation and median while Qualitative data were expressed in frequency and percent. Qualitative data were analyzed using Chi-square test also exact tests such as Fisher exact was applied to compare the two groups. Normally distributed quantitative data were analyzed using student t-test while quantitative data that were not normally distributed was analyzed using Mann Whitney test for comparing the two groups. p value equal or less than 0.05 was considered significant.

RESULTS

We studied 455 patients: 252 males, mean age 41 ± 15 years and APACHE II score 15.6 ± 6.2. The main syndrome diagnosis at admission was trauma (n= 75), neurocritical illness (n=77), respiratory failure (n=67), intoxication (n=87) sepsis (n=79), other diagnosis (n=70).

Patients were divided into two groups based upon their cumulative balance on first, third and fifth day of the study. Based upon that categorization of cases we monitored the parameters selected for the two groups and their progress on day one, day three and day five.

365 patients achieve positive balance at first day which represent 80% of cases with mean of 2104.6 ±1102.6 ml ,this percentage decrease in third day to 54% (246 patients) with mean of 2995 ± 5757.3 ml, while in fifth day 46% (210 patients) achieve positive balance with mean of 2159.6 ± 1145.3 ml . In other hand, 20% of cases (90 patients) achieve negative balance at first day with mean of 899.7 ± 409.6 ml then this percentage increase to 46% (209 patients) at third day with mean of 895.4 ± 412.1 ml while in fifth day 54 % (245 patients) achieve negative balance with mean of 1076.1± 495.9 ml. (Table 1).

Table-1.Distribution of studied sample according to fluid balance (n=455)

	1st Day (n= 455)		3rd Day (n= 455)		5th Day (n= 455)	
	No.	%	No.	%	No.	%
Fluid Balance						
Negative	**90**	**19.8**	**209**	**45.9**	**245**	**53.8**
Min. – Max.	500.0 – 2100.0		400.0 – 2500.0		200.0 – 3200.0	
Mean ± SD.	899.7 ± 409.6		895.4 ± 412.1		1076.1 ± 495.9	
Median	700.0		730.0		987.0	
Positive	**365**	**80.2**	**246**	**54.1**	**210**	**46.2**
Min. – Max.	300.0 – 6700.0		400.0 – 4210.0		553.0 – 5450.0	
Mean ± SD.	2104.6 ± 1102.6		2995.5 ± 5757.3		2159.6 ± 1145.3	
Median	2300.0		2000.0		2000.0	

Figure-1. Distribution of studied sample according to fluid balance

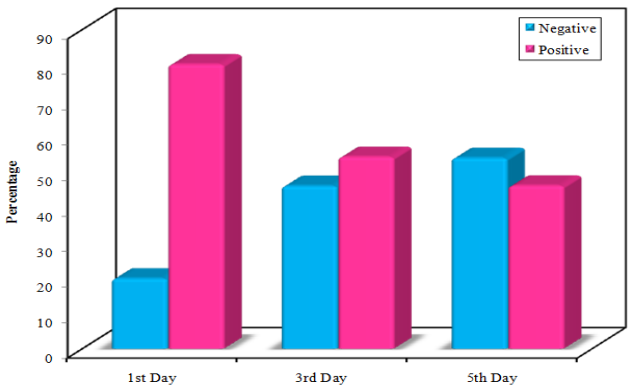


Table-2. Comparison between the two studied groups according to SOFA

	Fluid balance					
	1st Day		3rd Day		5th Day	
	Negative	Positive	Negative	Positive	Negative	Positive
SOFA	**(n = 89)**	**(n = 360)**	**(n = 205)**	**(n = 242)**	**(n = 245)**	**(n = 210)**
Min. – Max.	1.0 – 8.0	1.0 – 22.0	0.0 – 16.0	1.0 – 22.0	0.0 – 21.0	1.0 – 22.0
Mean ± SD.	5.8 ± 1.62	8.32 ± 4.56	5.59 ± 3.34	8.90 ± 4.44	4.75 ± 3.05	10.55 ± 5.16
Median	6.0	7.0	5.0	8.0	4.0	8.0
p	<0.001*		<0.001*		<0.001*	

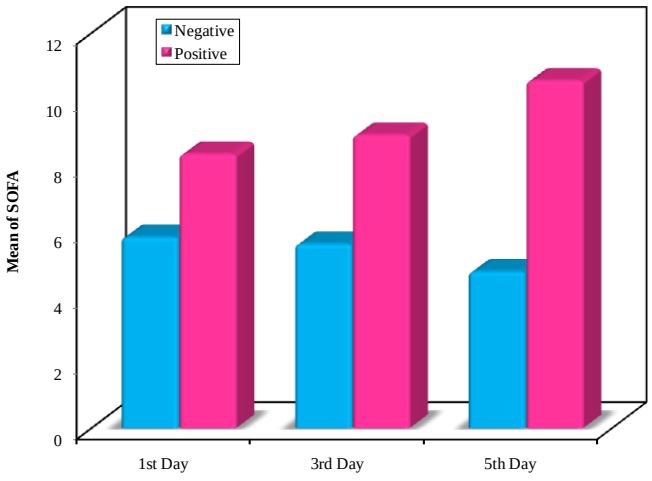
p: p value for Student t-test for comparing – ve and +ve fluid
*: Statistically significant at p ≤ 0.05

Table-3. Relation between fluid balance to outcome (total cases n=455)

	Fluid balance											
	1st Day				3rd Day				5th Day			
	Negative (n = 90)		Positive (n = 365)		Negative (n = 209)		Positive (n = 246)		Negative (n = 245)		Positive (n = 210)	
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
Outcome												
Death	25	27.8	188	51.5	55	26.3	158	64.2	33	13.5	180	85.7
Survival	65	72.2	177	48.5	154	73.7	88	35.8	212	86.5	30	14.3
p	<0.001*				<0.001*				<0.001*			
Ventilation days												
Min. – Max.	0.0 – 16.0		0.0 – 15.0		0.0 – 16.0		0.0 – 15.0		0.0 – 13.0		1.0 – 16.0	
Mean ± SD.	6.57 ± 3.02		6.57 ± 3.69		5.84 ± 3.55		7.19 ± 3.46		4.88 ± 3.02		8.55 ± 3.10	
Median	5.0		6.0		5.0		7.0		4.0		8.0	
p_1	0.987				<0.001*				<0.001*			
ICU days												
Min. – Max.	5.0 – 19.0		3.0 – 18.0		5.0 – 19.0		3.0 – 18.0		5.0 – 18.0		3.0 – 19.0	
Mean ± SD.	8.77 ± 2.90		8.47 ± 3.15		8.31 ± 3.02		8.72 ± 3.17		7.69 ± 2.77		9.52 ± 3.19	
Median	8.0		8.0		8.0		8.0		7.0		9.0	
p_1	0.424				0.162				<0.001*			

p: p value for Chi square test for comparing – ve and +ve fluid

Figure-2. Comparison between the two studied groups according to SOFA



Mean SOFA score for +ve balance cases was higher than that of + ve balance cases during whole study period, at first day (5.2 for -ve balance group compared to 8.3 for +ve balance group), in the third day (5.5 for -ve balance group compared to 8.9 for +ve balance group) and (4.7 for -ve balance group compared to 10.5 for +ve balance group) after fifth day. This difference was statistically significant (Table-2).

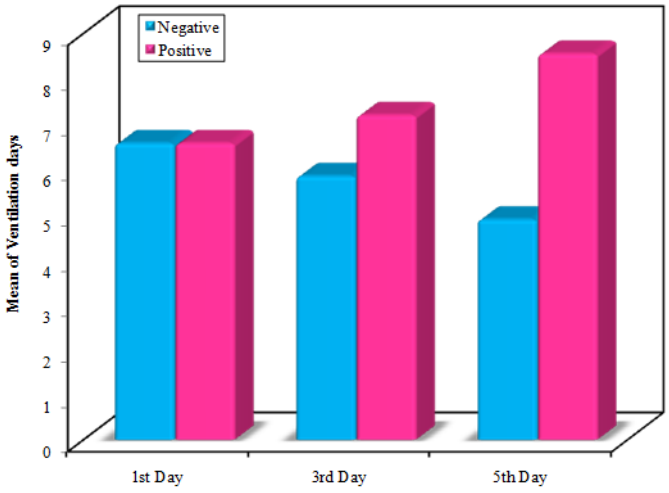
As regard the outcome data. First, according to 28 day mortality, Negative balance group had higher percentage of survival in comparison to positive balance group for all days of the study. (72% of -ve balance group compared to 48% of +ve balance group) in first day, this had increased in the third day (73% of -ve balance group compared to 35% of +ve balance group) and (86% of -ve balance group compared to 14% of +ve balance group after fifth day).

This difference was statistically significant in all days. Second, according to days on mechanical ventilator, Mean of ventilator days for both group was nearly equal in first day (6.5 day for both +ve balance

and –ve balance group) .However, this changed in third and fifth days as mean of ventilator days for +ve balance group higher than that of –ve balance group (7.1 for +ve balance group compared to 5.8 for –ve balance group) in third day and (8.5 for + ve balance group compared to 4.8 for –ve balance group) after fifth day. This difference was statistically significant in third and fifth days.

Third, according to length of ICU days. Mean ICU days was nearly equal for both group in first and third day. It was about 8 days for both group but this had changed in fifth day with mean of ICU days for +ve balance group became higher than that for –ve balance group (9.5 day for positive balance patients compared to 7.6 days for negative balance patients) and this was statistically. (Table 3).

Figure-3. Relation between fluid balance and mortality (total cases n=455)



Figur-4. Relation between fluid balance and Ventilation days

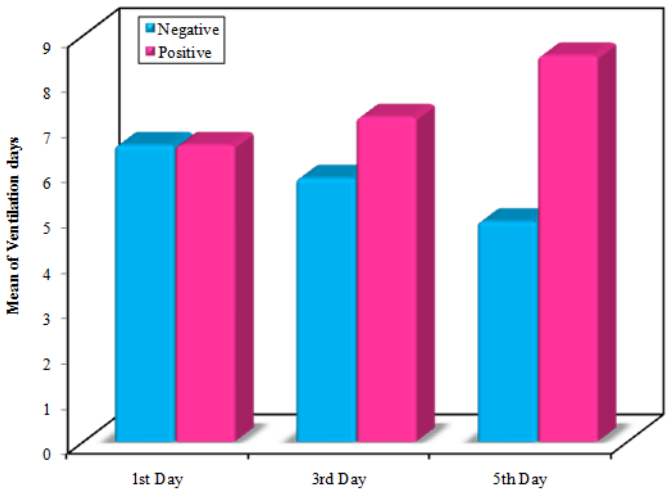
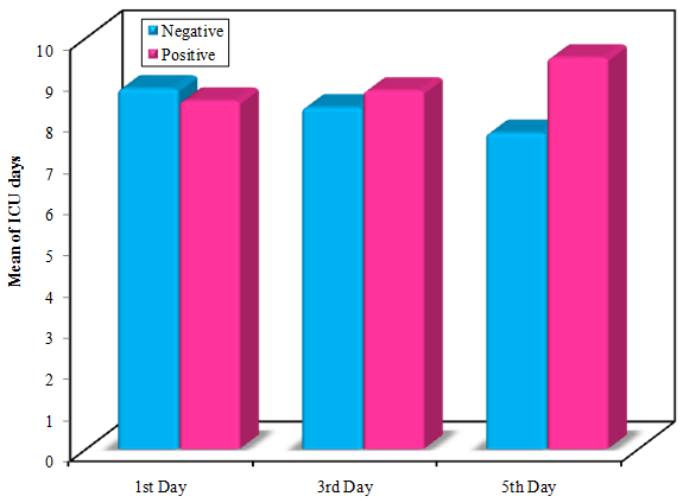


Figure-5. Relation between fluid balance and ICU days



Discussion

The amount of fluid during resuscitation of patients with critical illness is important. Too little fluid may result in tissue hypo-perfusion; however, too much fluid may result in volume accumulation. Several recent studies have demonstrated that a positive fluid balance in critical illness is associated with deteriorating outcomes. However, some studies have shown opposite results. The objective of this study was to determine the relation between fluid balance and ICU mortality in different ICU populations.

The results revealed that for all ICU patients, negative fluid balance on any day of the study is associated with better outcomes than for patients who do not achieve negative fluid balance with regards to SOFA score, mortality, duration of mechanical ventilation and length of ICU stay.

Our results are consistent with prior studies on critically ill patients. A positive fluid balance was strongly associated with increased mortality and other unfavorable outcomes in some subgroups of ICU patients, including worse lung function, longer duration of mechanical ventilation, increased post-operative complications and longer ICU stay.

A positive association between fluid balance and mortality is quite well established. Results from the SOAP study, an observational study of 3,147 adult patients from 198 European ICUs, indicated that, in patients with sepsis, fluid balance was an independent risk factor for mortality (6). Alsous et al. (8) also showed, in a single-center retrospective study of 36 patients with septic shock, that patients with a negative fluid balance (less than 500 ml) on at least 1 of the first 3 days after the onset of septic shock had better hospital survival. In ICU patients with sepsis or septic shock, Sirvent et al. (9) reported that the accumulated positive fluid balance at 48, 72, and 96 hours was

associated with higher mortality, and in a retrospective study, de Oliveira et al. (10) noted that a late (between 24 and 48 hours after diagnosis) positive fluid balance was an independent risk factor for mortality in severe sepsis. In a pediatric septic population, Abulebda et al. (11) showed that a positive fluid balance was associated with worse outcomes (increased mortality and complicated course) in patients with a low initial mortality risk but not in patients at moderate or high risk of death.

Better outcomes among patients with negative fluid balance could be explained by the following; since many critical diagnoses like severe sepsis are characterized by vasodilatation and capillary leak, which often leads to systemic hypo perfusion, successful resuscitation includes refilling the under filled system. Attenuation of the inflammatory cascade (of mediators) during successful treatment is expected to cause a return of normal vascular tone and the retrieval of fluid from the peripheral circulation and third space back to the central circulation. Excess fluid then should be eliminated via increased urine output, assuming that the heart and kidneys continue to function well.

Negative fluid balance may signal both the resolution of the hemodynamic derangements due to many critical diagnoses and that the kidneys and heart have not failed as a result of these insults. In this descriptive study, it is not possible to determine whether the positive fluid balance found in study population was the cause or the result of a greater severity of illness, especially as resuscitation protocols were not standardized and there is considerable debate as to the optimal approach to fluid management in critically ill patients. Thus, it is not surprising that the combination of these two signals portends a good prognosis and that negative fluid balance is not likely to be the cause of improved outcome but rather a marker for or an effect of the successful management of different critical illnesses. Clinicians should not seek to achieve negative fluid balance as an end in itself.

A point of strength in the present study is the choice of day one, three and five as critical days to assess whether or not a patient had achieved negative fluid balance (on any day) and the association between the balance and the outcomes. The rational is that an earlier assessment would be more meaningful to families and caretakers alike as a great percentage of ICU mortality occur before the third day. As for assessment of outcome at the third and fifth days, it can be argued that three days are a reasonable duration for a trial of therapy and five days for stabilization of patients' condition.

Another point of strength in the present study is the large sample size which allowed for stratification of outcome by diagnosis, studying the association of fluid balance with the outcome of specific diagnosis independently and increase the ability of the present study to assess the association of fluid balance with certain outcomes as weaning.

Our study has several important limitations. First, it was performed in a large teaching hospital and may not be generalizable to other types of institutions. However, the results are consistent with those demonstrated by other investigations suggesting that these findings are more generalizable. Second, a formal protocol for fluid management of critically ill patients wasn't present.

Finally, the methodology of this study, being a descriptive study based on review of the medical records limits our ability to determine a causal relationship between fluid management and the outcomes we evaluated and limits the extrapolation of these results to all patients. Thus it is recommended to conduct further randomized control and cohort studies before fluid balance is used to prognosticate and manage patients.

Conclusion

The impact of maintaining a negative fluid balance has been shown to improve outcomes in ICU patients with regards to SOFA score, mortality, and duration of mechanical ventilation and ICU length of stay.

Conflict of Interests

Authors declare that there is no conflict of interests regarding the publication of this paper.

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