Fluid Management in Critically Ill Patients

fluid overload: chicken or egg?

Bin Du, MD

Medical Intensive Care Unit

Peking Union Medical College Hospital

Presenter Disclosure Information

<Fluid Management in Critically Ill Patients: Fluid Overload, Chicken or Egg?>

I have no financial relationship to disclose.

Fluid Management in Critically Ill

Pros

- Hypovolemia common
  - Hypovolemia leads to hypoperfusion
  - Hypoperfusion contributes to organ dysfunction and/or death
- Fluid resuscitation corrects hypovolemia
  - Fluid resuscitation results in hemodynamic improvement
  - Fluid resuscitation improves clinical outcome

Cons

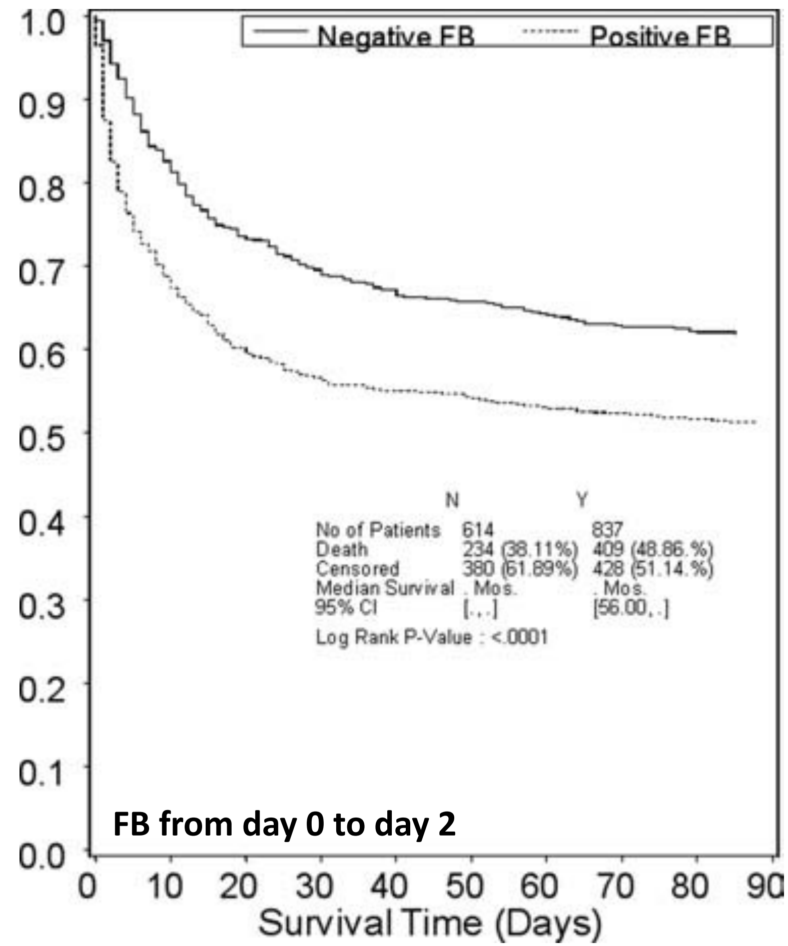
- Fluid overload leads to interstitial edema
  - Interstitial edema associated with impaired tissue oxygenation
  - Pulmonary edema impairs arterial oxygenation
- Fluid overload associated with poor clinical outcome

AKI/ARF on CVVH: Fluid Management

Retrospective analysis of data from 1453 patients enrolled in the RENAL study

Multivariate logistic regression analysis with death at 90 days after randomization as outcome

variable	OR (95%CI)	p
Negative mean daily fluid balance	0.318 (0.24 – 0.43)	< 0.0001
Age	1.033 (1.02 – 1.04)	< 0.0001
Time from ICU admission to randomization (d)	1.002 (1.00 – 1.04)	0.0065
APACHE III score	1.012 (1.01 – 1.02)	0.0002
SOFA score	1.224 (1.07 – 1.40)	0.0033
INR	1.277 (1.08 – 1.51)	0.0047



The RENAL Replacement Therapy Study Investigators. An observational study fluid balance and patient outcomes in the randomized evaluation of normal vs. augmented level of replacement therapy trial. Crit Care Med 2012; 40: 1753-1760

ALI/ARDS: Fluid Management

- 3,147 adult patients in 198 European ICUs in SOAP study
- 393 (12.5%) patients had ALI/ARDS
- ICU mortality 38.9%
- Hospital mortality 45.5%

variables	coefficient	mean, SE	OR (95%CI)	p value
cancer	1.473	0.521	4.4 (1.6-12.1)	0.005
High tidal volume	0.842	0.332	2.3 (1.2-4.4)	0.011
Mean SOFA score	0.353	0.052	1.4 (1.3-1.6)	< 0.001
Mean fluid balance	0.382	0.128	1.5 (1.1-1.9)	0.003

Sakr Y, Vincent JL, Reinhart K, et al. High tidal volume and positive fluid balance are associated with worse outcome in acute lung injury. Chest 2005; 128: 3098-3108

Fluid Balance in Acute Renal Failure

characteristic	hazard ratio	95%CI	P value
age	1.02	1.01 – 1.03	< 0.001
SAPS II (per point)	1.03	1.02 – 1.04	< 0.001
heart failure	1.38	1.05 – 1.81	0.02
medical admission	1.68	1.35 – 2.08	< 0.001
mean fluid balance, L/24 h	1.21	1.13 – 1.28	< 0.001
mechanical ventilation	1.55	1.14 – 2.11	< 0.001
liver cirrhosis	2.73	1.88 – 3.95	< 0.001

Payen D, de Pont AC, Sakr Y, et al. A positive fluid balance is associated with a worse outcome in patients with acute renal failure. Crit Care 2008; 12: R74

Fluid Overload in Critically Ill Children

- 113 critically ill children receiving CVVH
- %fluid overload 10.9 (2.8, 22.1)
- Acute fluid overload as indication of CVVH in 37% patients
- Fluid overload as independent predictor of mortality
  - All patients OR 1.37, 95%CI 0.97 – 1.94, p = 0.07
  - MODS OR 1.30, 95%CI 0.92 – 1.84, p = 0.13
  - ≥ 3 organ failure OR 1.78, 95%CI 1.13 – 2.82, p = 0.01

$$\text{Fluid overload (\%)} = \frac{\text{Total fluid intake} - \text{total fluid output (L)}}{\text{Body weight (kg)}}$$

Foland JA, Fortenberry JD, Warshaw BL, et al. Fluid overload before continuous hemofiltration and survival in critically ill children: a retrospective analysis. Crit Care Med 2004; 32: 1771-1776

Fluid Overload Predicts Mortality in Non-AKI

- Septic shock
  - Net negative fluid balance ≥ 500 ml within the first 3 days of ICU admission predicted survival (100% vs. 20%)
  - Both adequate initial fluid bolus and conservative late fluid management associated with the lowest hospital mortality (18.3% vs. 77.1%)
  - Mean fluid balance during the first 72 hrs of ICU admission as a significant independent outcome predictor (OR 1.1)
- ALI/ARDS
  - Conservative fluid management strategy resulted in significant increase in ventilator-free days and ICU-free days, despite no different in mortality
    - average total fluid balance within the first week -136 ml vs. +6992 ml

Cerda J, Sheinfeld G, Ronco C. Fluid overload in critically ill patients with acute kidney injury. Blood Purif 2010; 29: 11-18

Fluid Overload Predicts Mortality in AKI

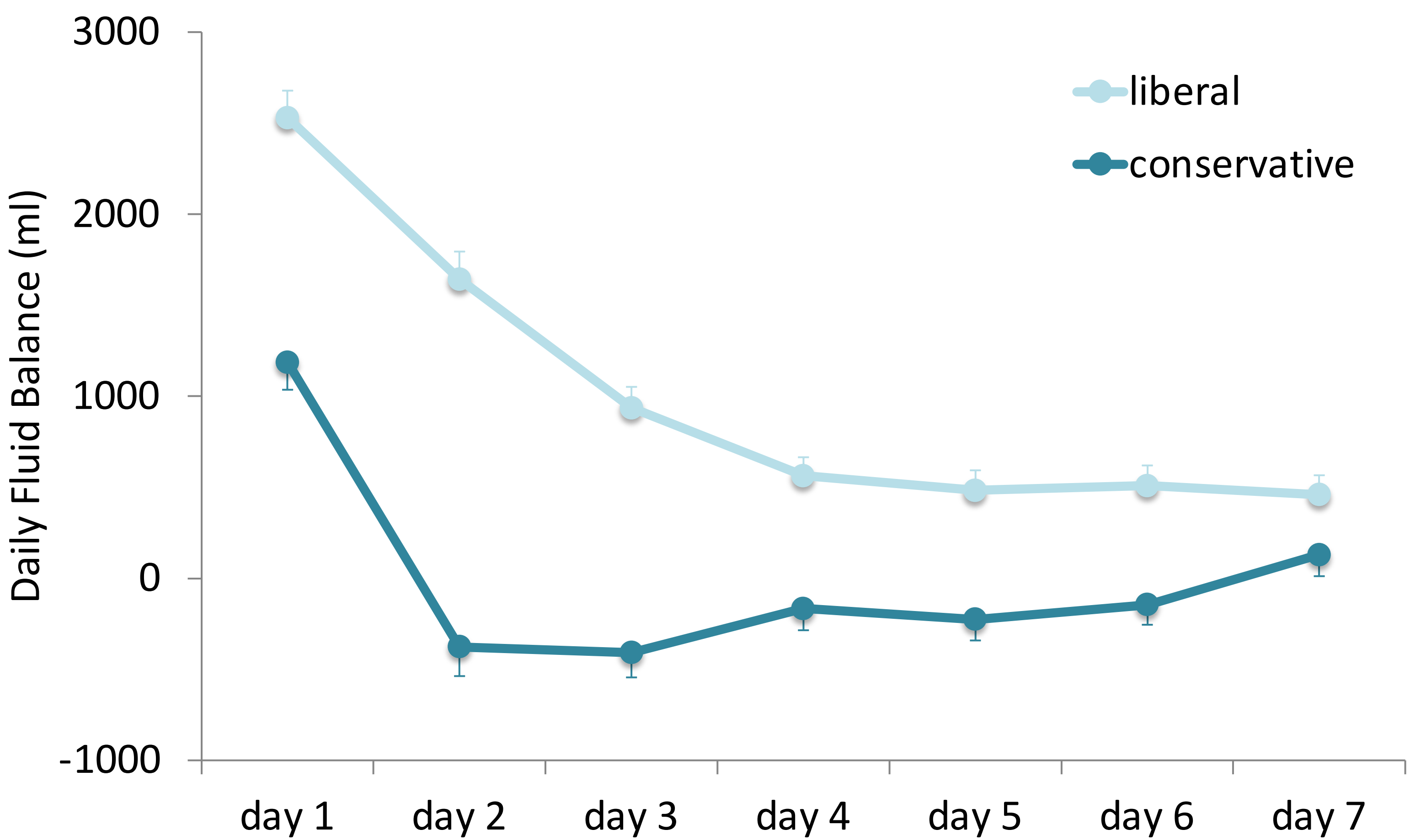
- SOAP study
  - mean daily fluid balance as an independent mortality predictor (OR 1.21), while significantly higher daily fluid balance in oliguric patients and dialyzed patients
- PICARD study
  - association of fluid overload with survival both in patients on dialysis and patients on conservative treatment
  - superiority of CRRT over IHD in achieving net fluid removal in AKI
  - extent of fluid overload during AKI influences renal recovery

Cerda J, Sheinfeld G, Ronco C. Fluid overload in critically ill patients with acute kidney injury. Blood Purif 2010; 29: 11-18

Fluid Overload Associated With Mortality

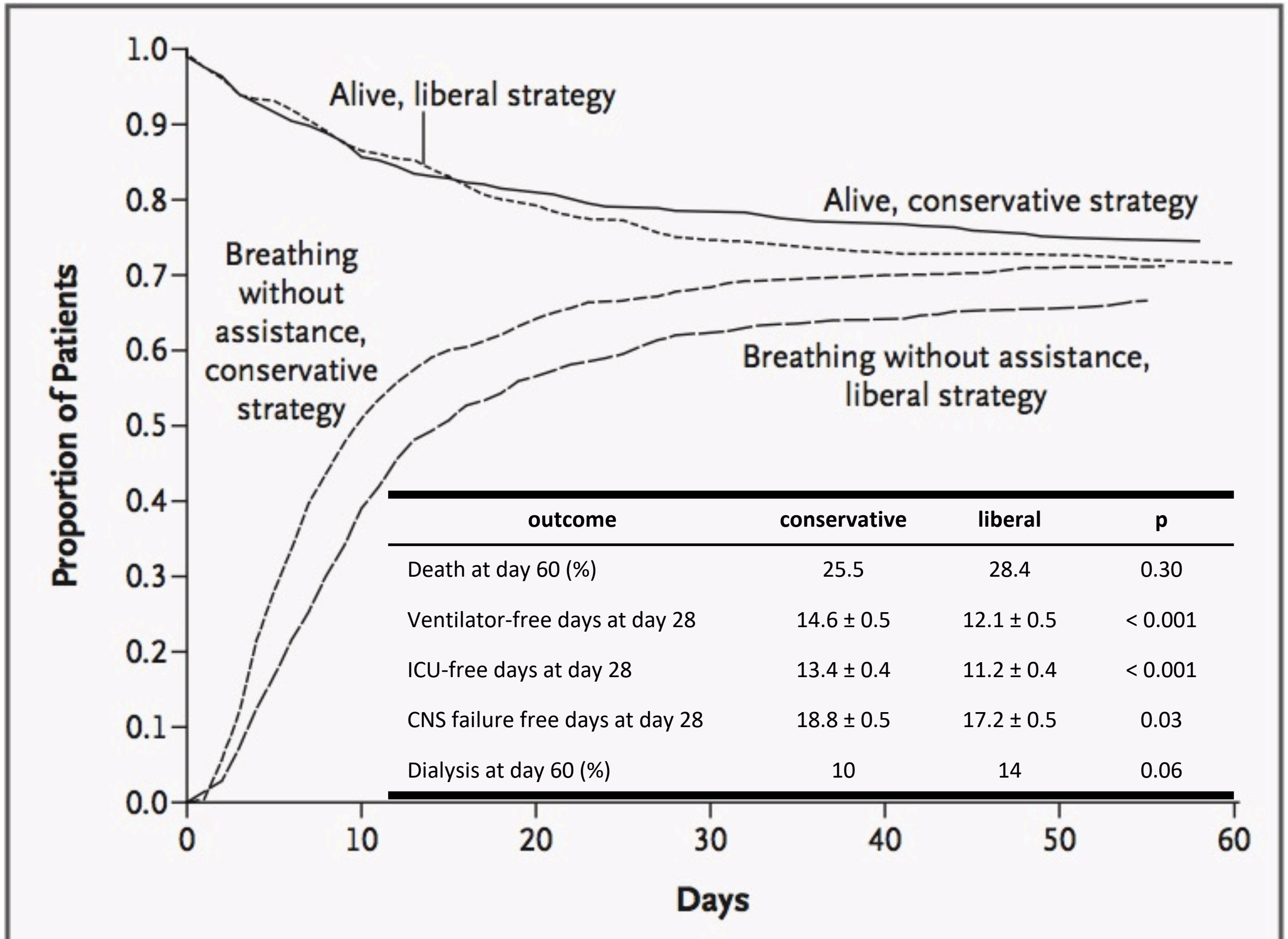
- Adults
  - Positive fluid balance associated with mortality in
    - ALI/ARDS
    - AKI
    - Septic shock
  - Late positive fluid balance associated with mortality in ARDS and shock
- Pediatrics
  - Fluid overload before CRRT associated with higher mortality
  - More weight gain associated with mortality in BMT recipients

Conservative Fluid Management in ALI



The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 2006; 354: 2564-2575

Conservative Fluid Management in ALI



outcome	conservative	liberal	p
Death at day 60 (%)	25.5	28.4	0.30
Ventilator-free days at day 28	14.6 ± 0.5	12.1 ± 0.5	< 0.001
ICU-free days at day 28	13.4 ± 0.4	11.2 ± 0.4	< 0.001
CNS failure free days at day 28	18.8 ± 0.5	17.2 ± 0.5	0.03
Dialysis at day 60 (%)	10	14	0.06

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 2006; 354: 2564-2575

Albumin & Furosemide in ALI

- Inclusion criteria
  - AECC definition for ALI
  - Serum total protein ≤ 5 g/dL
  - Ongoing nutritional support
  - Mechanical ventilation ≥ 48 h
- Exclusion criteria
  - Hemodynamic instability
  - Renal disease
  - Hepatic failure
  - Allergies to study drugs
  - Pregnancy
  - Na > 150 mEq/L
  - K < 2.5 mEq/L
- Treatment group
  - Furosemide iv titrated (max 8 mg/hr) to achieve net diuresis and daily weight loss ≥ 1 kg
  - 25% albumin 25 g iv q8h until serum total protein > 6.0 g/dL
  - Duration 5 days
- Control group
  - Double placebo

Martin GS, Mangialardi RJ, Wheeler AP, et al. Albumin and furosemide therapy in hypoproteinemic patients with acute lung injury. Crit Care Med 2002; 30: 2175-2182

Albumin & Furosemide in ALI

	Placebo (n = 18)	Treatment (n = 19)	All (n = 37)
Age, yrs	42.5 ± 18.0	42.3 ± 15.9	42.4 ± 16.8
Male sex, %	74	53	65
Surgical service, n (%)	16 (89)	13 (68)	29 (78)
Trauma	15	13	28
Pneumonia	1	5	6
Sepsis	1	1	2
Aspiration	1	0	1
LIS	2.6 (0.4)	2.6 (0.6)	2.6 (0.5)
APACHE III score	55.8 (20.8)	61.1 (22.2)	58.5 (21.4)
Serum total protein, g/dL	4.0 (0.5)	3.9 (0.6)	4.0 (0.5)
Serum albumin, g/dL	1.7 (0.3)	1.8 (0.3)	1.8 (0.3)

Patients in both groups were admitted to ICU a median of 4.0 days (IQR 3.0 – 6.0 days) before study enrollment

Martin GS, Mangialardi RJ, Wheeler AP, et al. Albumin and furosemide therapy in hypoproteinemic patients with acute lung injury. Crit Care Med 2002; 30: 2175-2182

Albumin & Furosemide in ALI

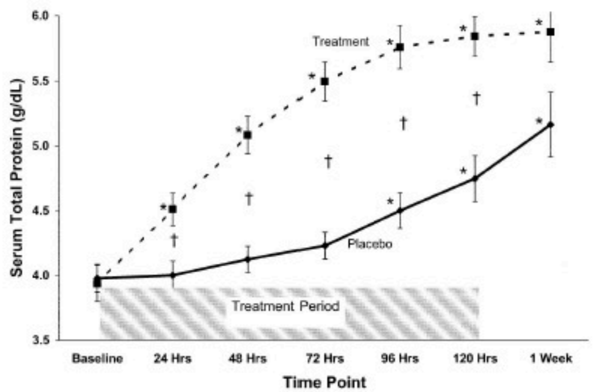


Figure 1. Change in serum total protein during the study, with the treatment period identified by the *shaded area. Points* represent mean, with *error bars* indicating SEM. *Significant within-group change from baseline; †time points with significant between-group differences.

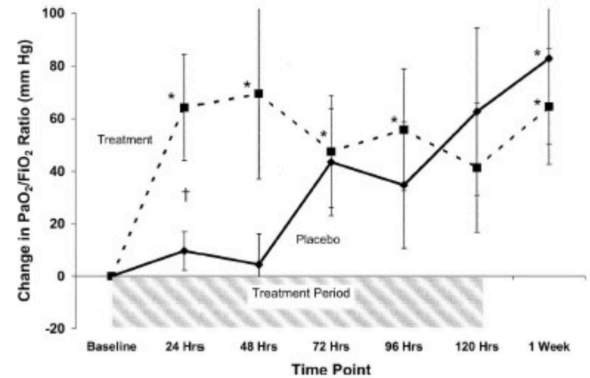


Figure 3. Change in oxygenation, as measured by the PaO_2/FiO_2 ratio (mean ± SEM), with the treatment period identified by the *shaded area.* *Significant within-group change from baseline; †time points with significant between-group differences. A maximum of 25% of data points may be absent from calculations represented after day 5.

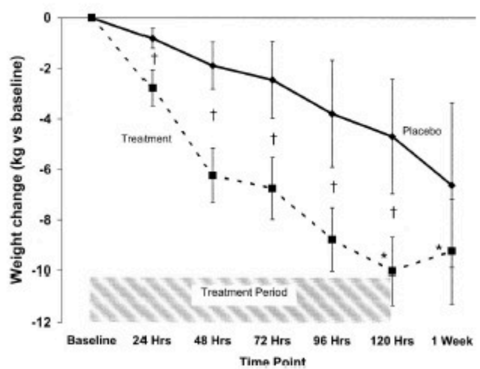


Figure 2. Weight loss observed (mean ± SEM) during the 5-day study period. *Significant within-group change from baseline; †time points with significant between-group differences. The *shaded area* indicates the treatment period.

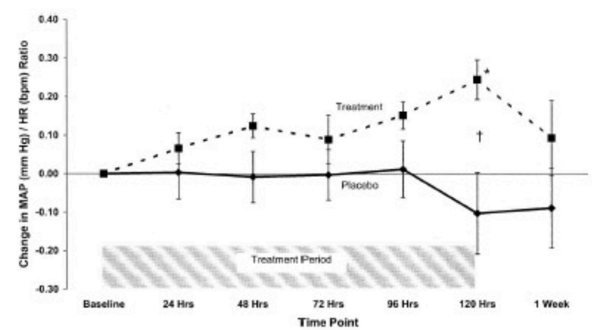


Figure 4. Change in the mean arterial pressure (mm Hg)/heart rate (beats/min) ratio (*MAP/HR* ratio) from baseline. The treatment period is indicated by the *shaded area. Points* represent mean values, with *error bars* depicting SEM (mean ± SEM) at each time point. *Significant within-group change from baseline; †time points with significant between-group differences.

Martin GS, Mangialardi RJ, Wheeler AP, et al. Albumin and furosemide therapy in hypoproteinemic patients with acute lung injury. Crit Care Med 2002; 30: 2175-2182

Albumin & Furosemide in ALI

- study design:
  - a randomized, double-blinded, placebo-controlled multicenter trial
- subjects:
  - 40 mechanically ventilated ALI/ARDS patients with serum total protein < 6.0 g/dL
- intervention:
  - 25% albumin 25 g q8h (until serum total protein > 8.0 g/dL) + furosemide iv (titrated to achieve a net negative fluid balance and daily weight loss ≥ 1 kg, with max. 10 mg/hr) x 3 days
  - Placebo
- primary outcome:
  - change in oxygenation over a 24-hr period

Martin GS, Moss M, Wheeler AP, et al. A randomized, controlled trial of furosemide with or without albumin in hypoproteinemic patients with acute lung injury. Crit Care Med 2005; 33: 1681-1687

Albumin & Furosemide in ALI

- patient characteristics
  - 65% from medical ICU
  - sepsis (38%) and trauma (25%) as the most common cause of ALI
  - developed ALI a median of 3 days (IQR 1.0 – 5.0 days) before study enrollment
- results
  - greater increase in PaO_2/FiO_2 in treatment group (+43 vs. -24 mmHg at 24 h, and +49 vs. -13 mmHg at day 3)
  - greater increase in serum total protein (1.5 vs. 0.5 g/dL at day 3) in treatment group
  - greater increase in net fluid loss (-5480 vs. -1490 ml at day 3) in treatment group
- conclusions
  - the addition of albumin to furosemide therapy in hypoproteinemic patients with ALI/ARDS significantly improves oxygenation, with greater net negative fluid balance and better maintenance of hemodynamic stability.

Martin GS, Moss M, Wheeler AP, et al. A randomized, controlled trial of furosemide with or without albumin in hypoproteinemic patients with acute lung injury. Crit Care Med 2005; 33: 1681-1687

Conservative Fluid Management

Negative Fluid Balance in Septic Shock

- At least 1 day of net negative fluid balance (> 500 ml) in the first 3 days of treatment strongly predicted survival across the strata of
  - Age
  - APACHE II score
  - First-day SOFA score
  - Third-day SOFA score
  - The need for mechanical ventilation
  - Creatinine level at ICU admission

Alsous F, Khamiees M, DeGirolamo A, et al. Negative fluid balance predicts survival in patients with septic shock: a retrospective pilot study. Chest 2000; 117: 1749-1754

Negative Fluid Balance in Septic Shock

- This study was not a trial of therapy aimed at producing negative fluid balance, but rather an observational study demonstrating that its occurrence is associated with improved outcome.
- …fluid management should continue with the aim of repleting the intravascular space, and a goal of inducing negative fluid balance is not warranted at this time.

Varon J, Fromm RE. Fluid balance in sepsis: are we ready for a negative balance? Chest 2000; 117: 1535-1536

Fluid Overload: Chicken or Egg?

Cerda J, Sheinfeld G, Ronco C. Fluid overload in critically ill patients with acute kidney injury. Blood Purif 2010; 29: 11-18

ALI & Septic Shock: Evidence of Fluid Management

- Methods: a retrospective analysis
- Settings: Barnes-Jewish Hospital (St. Louis, MO) and the medical ICU of Mayo Medical Center (Rochester, MN)
- Patients: patients hospitalized with septic shock and development of ALI within 72 h of septic shock onset
- Definitions:
  - Adequate initial fluid resuscitation (AIFR): the administration of an initial fluid bolus of > 20 mL/kg prior to and achievement of CVP > 8 mm Hg within 6 h after the onset of therapy with vasopressors
  - Conservative late fluid management (CLFM): even-to-negative fluid balance measured on at least 2 consecutive days during the first 7 days after septic shock onset

Murphy CV, Schramm GE, Doherty JA, et al. The importance of fluid management in acute lung injury secondary to septic shock. Chest 2009; 136: 102-109

ALI & Septic Shock: Evidence of Fluid Management

	Survivors (n = 125)	Nonsurvivors (n = 87)	P value
Initial fluid resuscitation			
Volume within 6 h of septic shock onset			
ml	**3,500 (1,825-6,000)**	**3,000 (1,000-4,500)**	**0.076**
ml/kg	45.5 (20.5-89.5)	42.9 (13.4-64.6)	0.132
CVP measured	115 (92.0)	61 (70.1)	< 0.001
AIFR	99 (79.2)	47 (54.0)	< 0.001
$ScvO_2$ measured	57 (45.6)	34 (39.1)	0.345
$ScvO_2 \geq 70\%$	40 (32.0)	30 (34.5)	0.705
Colloids administered	59 (47.2)	53 (60.9)	0.049
PRBCs administered	87 (69.6)	71 (81.6)	0.048

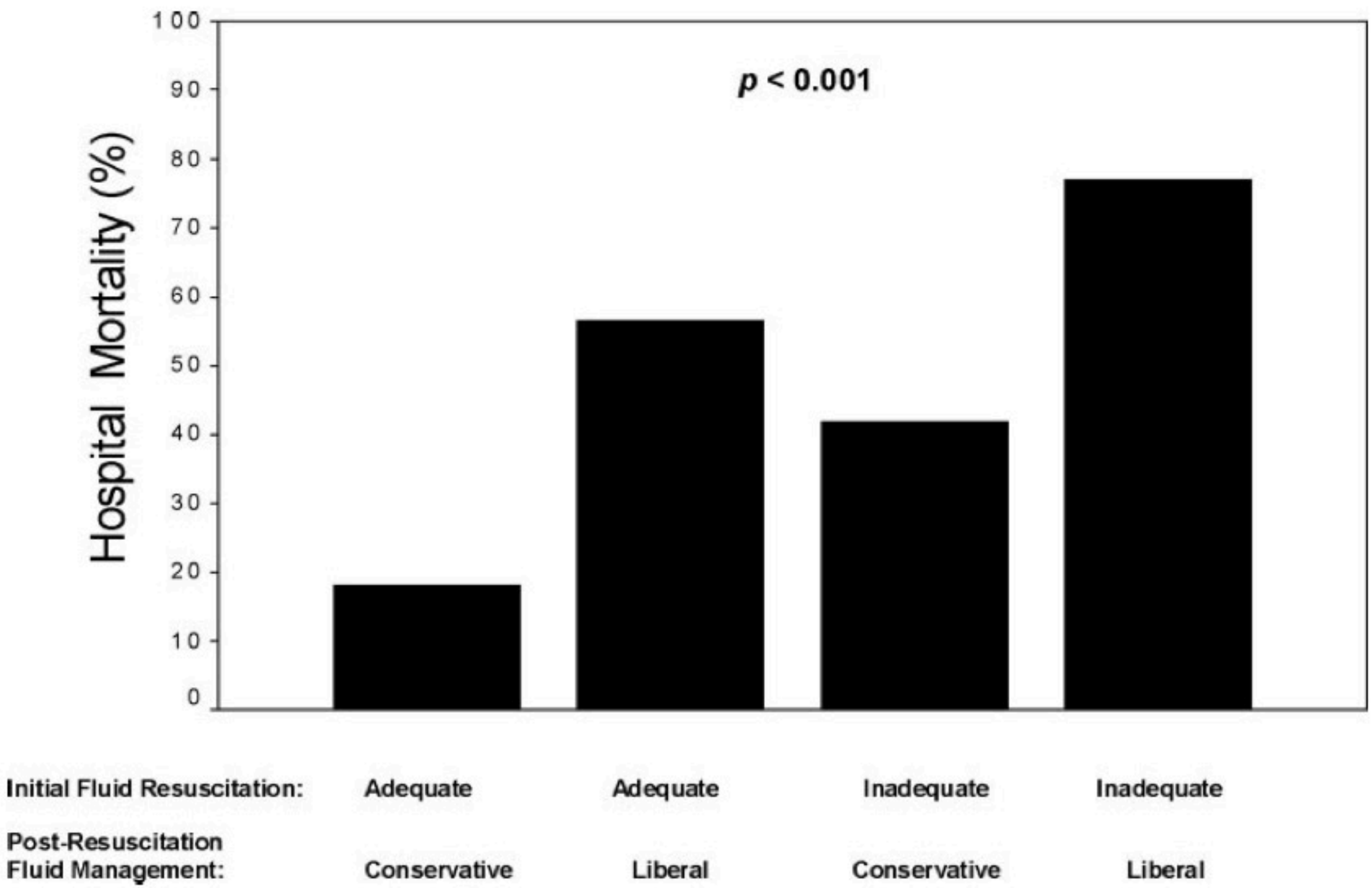
Murphy CV, Schramm GE, Doherty JA, et al. The importance of fluid management in acute lung injury secondary to septic shock. Chest 2009; 136: 102-109

ALI & Septic Shock: Evidence of Fluid Management

	Survivors (n = 125)	Nonsurvivors (n = 87)	P value
Late fluid management			
cumulative 7-day fluid balance, ml	**8,062 (2,412-13,833)**	**13,694 (7,113-20,249)**	**< 0.001**
CLFM	91 (72.8)	30 (34.5)	< 0.001
ICU fluid balance, ml	8,037 (2,487-13,575)	19,335 (9,765-27,274)	< 0.001
hospital fluid balance, ml	6,603 (-547-14,026)	22,231 (11,643-30,682)	< 0.001
appropriate initial antimicrobial therapy in patients with positive cultures	43 (70.5)	24 (61.5)	0.353
corticosteroids	70 (56.0)	50 (57.5)	0.832
drotrecogin alpha activated	9 (7.2)	7 (8.0)	0.799

Murphy CV, Schramm GE, Doherty JA, et al. The importance of fluid management in acute lung injury secondary to septic shock. Chest 2009; 136: 102-109

ALI & Septic Shock: Fluid Management



Murphy CV, Schramm GE, Doherty JA, et al. The importance of fluid management in acute lung injury secondary to septic shock. Chest 2009; 136: 102-109

ALI & Septic Shock: Evidence of Fluid Management

	Adjusted OR	95%CI	P value
APACHE II score*	1.07	1.01-1.14	0.030
Charlson comorbidity score*	1.11	1.01-1.23	0.040
Renal replacement therapy	3.15	1.51-4.79	0.020
Colloid administration	2.94	1.41-4.47	0.011
AIFR not achieved	**4.94**	**2.07-11.79**	**< 0.001**
Duration of vasopressors**	1.24	1.04-1.47	0.017
CLFM not achieved	**6.13**	**2.77-13.57**	**< 0.001**

*, 1-point increments
**, 1-day increments

Murphy CV, Schramm GE, Doherty JA, et al. The importance of fluid management in acute lung injury secondary to septic shock. Chest 2009; 136: 102-109

Positive Fluid Balance in Septic Shock

CVP group	12-hr net fluid balance: Survivors	12-hr net fluid balance: Nonsurvivors	p
All patients	3444 (1861-5984) ml	4429 (2537-6560) ml	< .001
CVP < 8 mmHg	3015 (1296-4987) ml	2281 (802-5711) ml	NS
CVP 8 – 12 mmHg	2727 (1227-5491) ml	3112 (1559-4809) ml	NS
CVP > 12 mmHg	3975 (2387-6614) ml	5237 (3140-7773) ml	< .001

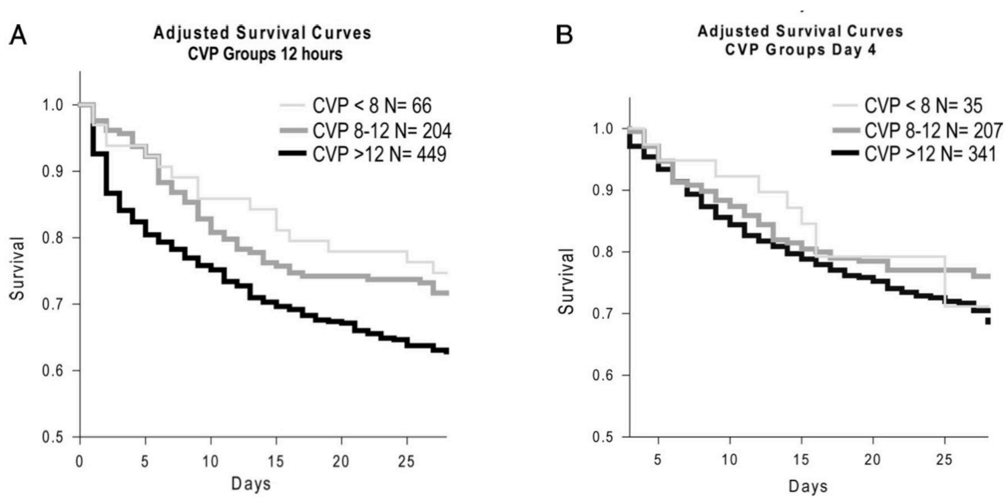


Table 3. Hazard ratio for death according to CVP group

CVP Group	Adjusted Hazard Ratio versus CVP >12 mm Hg
12 hrs	
CVP <8 mm Hg	0.606 (0.363–0.913)
CVP 8–12 mm Hg	0.762 (0.562–0.943)
Day 4	
CVP <8 mm Hg	0.903 (0.484–1.686)
CVP 8–12 mm Hg	0.764 (0.542–1.078)

CVP, central venous pressure.
Hazard ratios are shown with their 95% confidence intervals.

Boyd JH, Forbes J, Nakada T, et al. Fluid resuscitation in septic shock: a positive fluid balance and elevated central venous pressure are associated with increased mortality. Crit Care Med 2011; 39: 259-265

Conservative Fluid Management in ALI Does Not Necessarily Mean Diuresis

Measured intravascular pressure (mm Hg)				MAP <60 mm Hg or a need for any vasopressor (except dopamine ≤5 μg/kg/min); consider correctable causes of shock first	MAP ≥60 mm Hg without vasopressors (except dopamine ≤5 μg/kg/min)			
CVP		PAOP[G]			Average urinary output <0.5 ml/kg/hr		Average urinary output ≥0.5 ml/kg/hr	
Conservative strategy	Liberal strategy	Conservative strategy	Liberal strategy		**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index ≥2.5 liters/min/m² or absence of criteria for ineffective circulation	**Ineffective Circulation** Cardiac index <2.5 liters/min/m² or cold, mottled skin with capillary-refilling time >2 sec	**Effective Circulation** Cardiac index ≥2.5 liters/min/m² or absence of criteria for ineffective circulation
Range 1				1 Vasopressor[F] Fluid bolus[F]	3 KVO IV Dobutamine[A] Furosemide[B,1,2,4]	7 KVO IV Furosemide[B,1,2,4]	11 KVO IV Dobutamine[A] Furosemide[B,1,3,4]	15 KVO IV Furosemide[B,1,3,4]
>13	>18	>18	>24					
Range 2					4 KVO IV Dobutamine[A]	8 KVO IV Furosemide[B,1,2,4]	12 KVO IV Dobutamine[A]	16 KVO IV Furosemide[B,1,3,4]
9–13	15–18	13–18	19–24					
Range 3				2 Fluid bolus[F] Vasopressor[F]	5 Fluid bolus[C]	9 Fluid bolus[C]	13 Fluid bolus[C]	17 Liberal KVO IV
4–8	10–14	8–12	14–18					18 Conservative Furosemide[B,1,3,4]
Range 4					6 Fluid bolus[C]	10 Fluid bolus[C]	14 Fluid bolus[C]	19 Liberal fluid bolus
<4	<10	<8	<14					20 Conservative KVO IV

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 2006; 354: 2564-2575

Conservative Fluid Management in ALI Does Not Necessarily Mean Diuresis

- A 50-yo Caucasian male patient
- ALI/ARDS due to pneumonia
  - PaO_2/FiO_2 155 mmHg
  - PEEP 9 – 10 cmH_2O
- Hemodynamics
  - CVP ≤ 8 mmHg and/or PAOP ≤ 12 mmHg
  - CI ≥ 2.5 $L/min/m^2$
  - absence of criteria for ineffective circulation (cold, mottled skin with capillary refilling time > 2 sec)
- Further hemodynamic management?
  - fluid bolus?
  - diuresis?

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. N Engl J Med 2006; 354: 2564-2575

Albumin & Furosemide in ALI

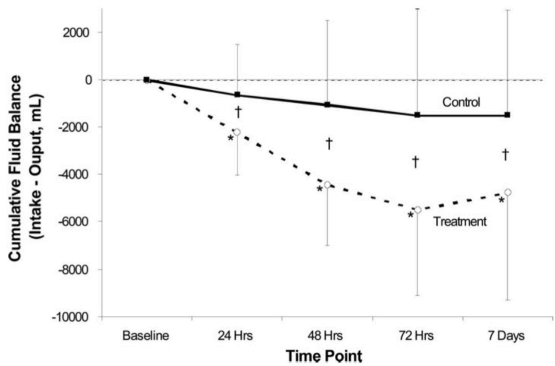


Figure 3. Cumulative fluid balance during the study period, comparing patients treated with furosemide and albumin (treatment, *dashed line*) or furosemide and placebo (control, *solid line*). *Points* are mean values with error bars depicting standard error of the mean (mean ± SD) at each time point. *Significant differences from baseline; †significant between-group differences at $p < .05$.

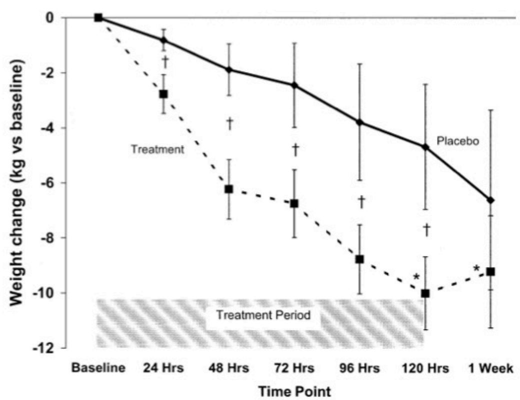


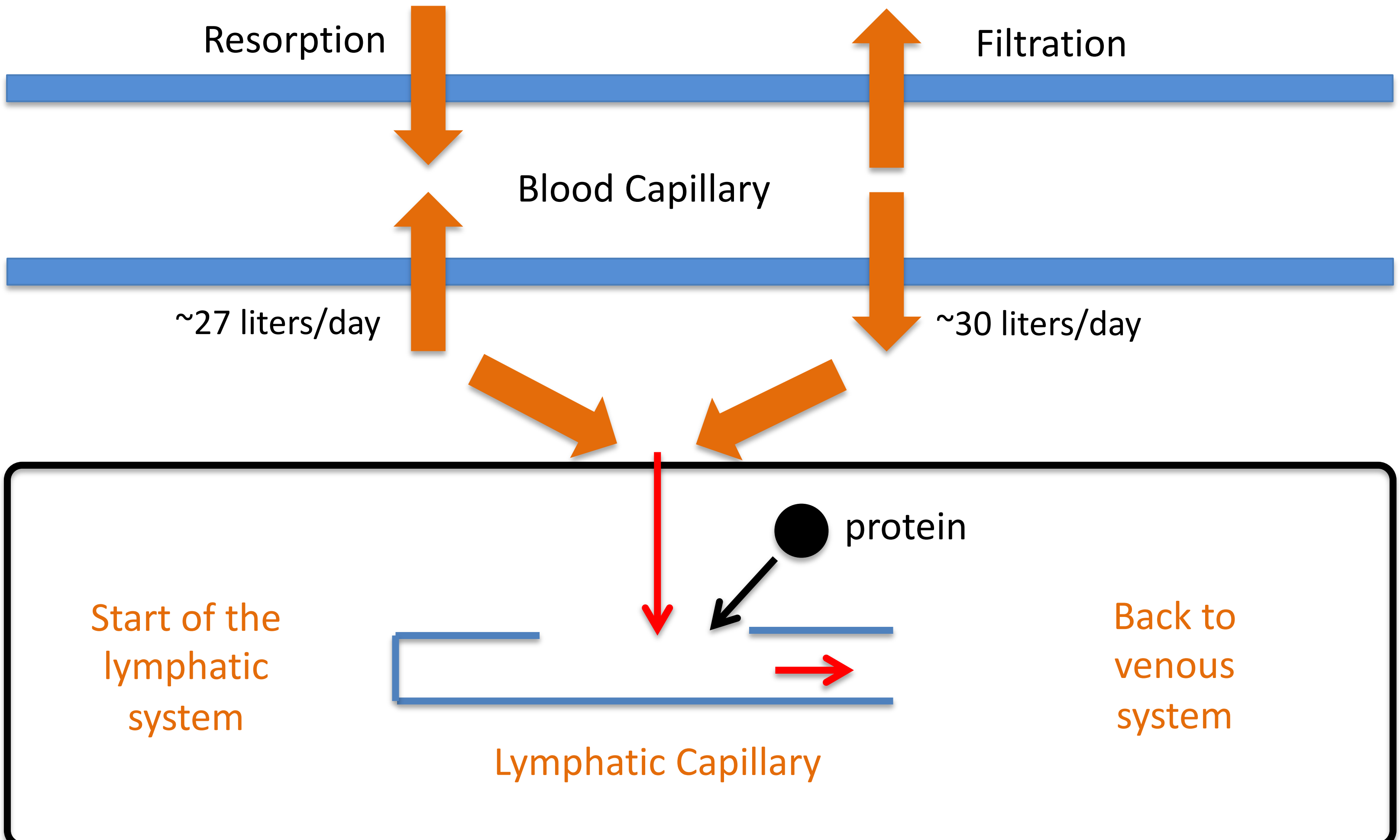
Figure 2. Weight loss observed (mean ± SEM) during the 5-day study period. *Significant within-group change from baseline; †time points with significant between-group differences. The *shaded area* indicates the treatment period.

- Only placebo or control group tells you what happened in enrolled patients
- When does ALI/ARDS patients exhibit the following without albumin repletion and/or aggressive diuresis?
  - Negative fluid balance
  - Reduction of body weight
  - Increase of serum albumin
  - Improvement of arterial oxygenation

Martin GS, Mangialardi RJ, Wheeler AP, et al. Albumin and furosemide therapy in hypoproteinemic patients with acute lung injury. Crit Care Med 2002; 30: 2175-2182

Martin GS, Moss M, Wheeler AP, et al. A randomized, controlled trial of furosemide with or without albumin in hypoproteinemic patients with acute lung injury. Crit Care Med 2005; 33: 1681-1687

Normal Fluid Balance: When Physiology Applies



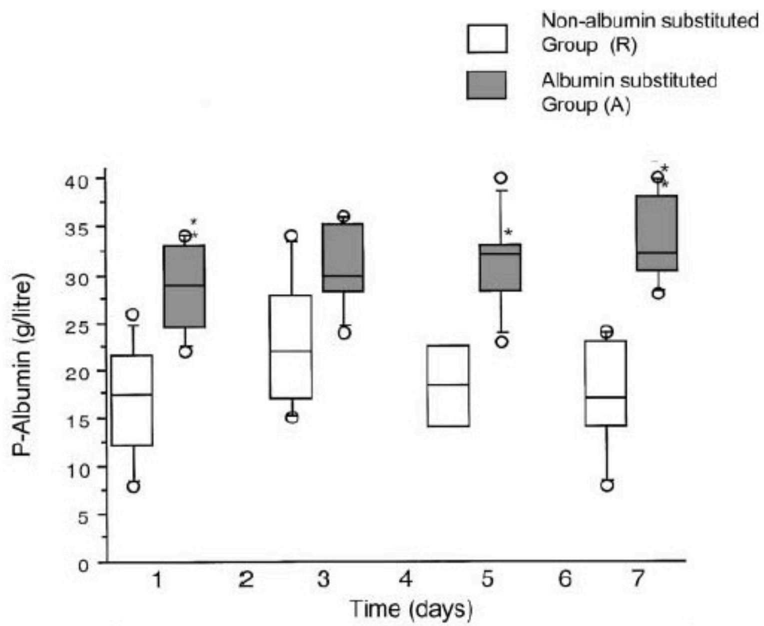
Albumin Does Not Mobilize Tissue Edema

18 consecutive patients with 18 – 90% BSA burn

- group A (Albumin): albumin target level ≥ 30 g/L
- group R (Ringer)

16 healthy male control subjects

Fig. 7 Plasma albumin concentrations in the two treatment groups (Ringer or albumin supplementation) 1, 3, 5 and 7 days post-burn. $^{*}P < 0.05$ and $^{**}P < 0.01$. Box plots with the five horizontal lines showing 10, 25, 50 (median), 75, and 90th centiles. Outliers are shown as *circles*. In the table is shown (mean ± SEM) albumin supplementation to the albumin group (g/patient/day)



Albumin to group A (g/pat./day)	69±21	73±25	60±17	34±18	49±19	51±18	31±12

Zdolsek HJ, Lisander B, Jones AW, et al. Albumin supplementation during the first week after a burn does not mobilise tissue oedema in humans. Intensive Care Med 2001; 27: 844-852

Albumin Does Not Mobilize Tissue Edema

18 consecutive patients with 18 – 90% BSA burn
- group A (Albumin): albumin target level ≥ 30 g/L
- group R (Ringer)

16 healthy male control subjects

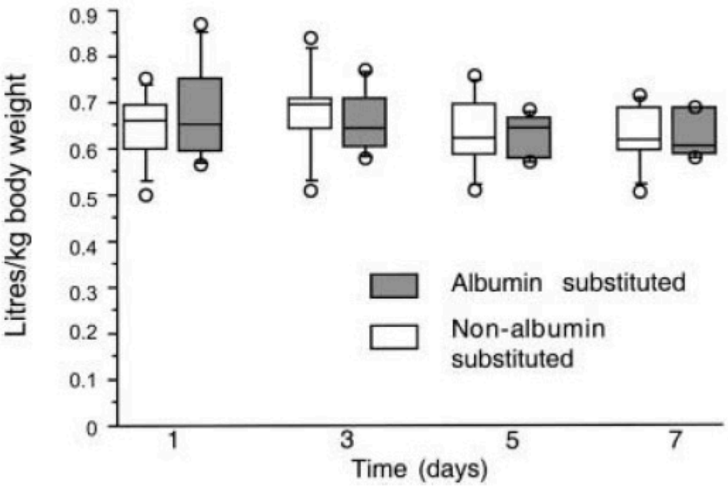


Fig. 8 Total body water measured by ethanol dilution in the two different treatment groups (Ringer or albumin supplementation). Box plots with the five horizontal lines showing 10, 25, 50 (median), 75, and 90th centiles. Outliers are shown as *circles*

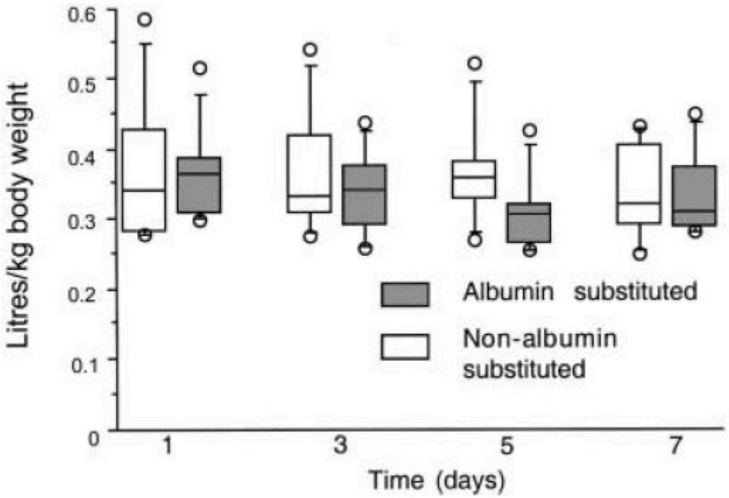


Fig. 9 Estimated extracellular water (iohexol dilution) in the two different treatment groups (Ringer or albumin supplementation). Box plots with the five horizontal lines showing 10, 25, 50 (median), 75, and 90th centiles. Outliers are shown as circles

Zdolsek HJ, Lisander B, Jones AW, et al. Albumin supplementation during the first week after a burn does not mobilise tissue oedema in humans. Intensive Care Med 2001; 27: 844-852

Albumin Does Not Mobilize Tissue Edema

- 18 consecutive patients with 18 – 90% BSA burn
  - group A (Albumin): albumin target level ≥ 30 g/L
  - group R (Ringer)
- 16 healthy male control subjects

- Conclusion: Body water increases after a burn. Excess water is mainly deposited in the extracellular space. Tissue oedema fluid is not mobilised by albumin supplementation.

Zdolsek HJ, Lisander B, Jones AW, et al. Albumin supplementation during the first week after a burn does not mobilise tissue oedema in humans. Intensive Care Med 2001; 27: 844-852

Effect of Diuresis on Lung Water

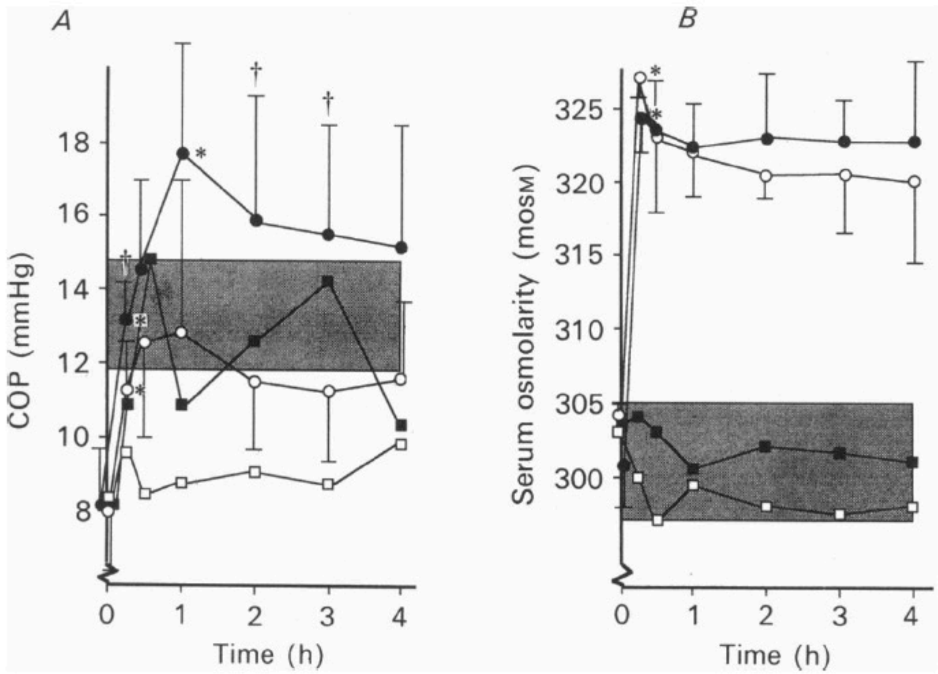
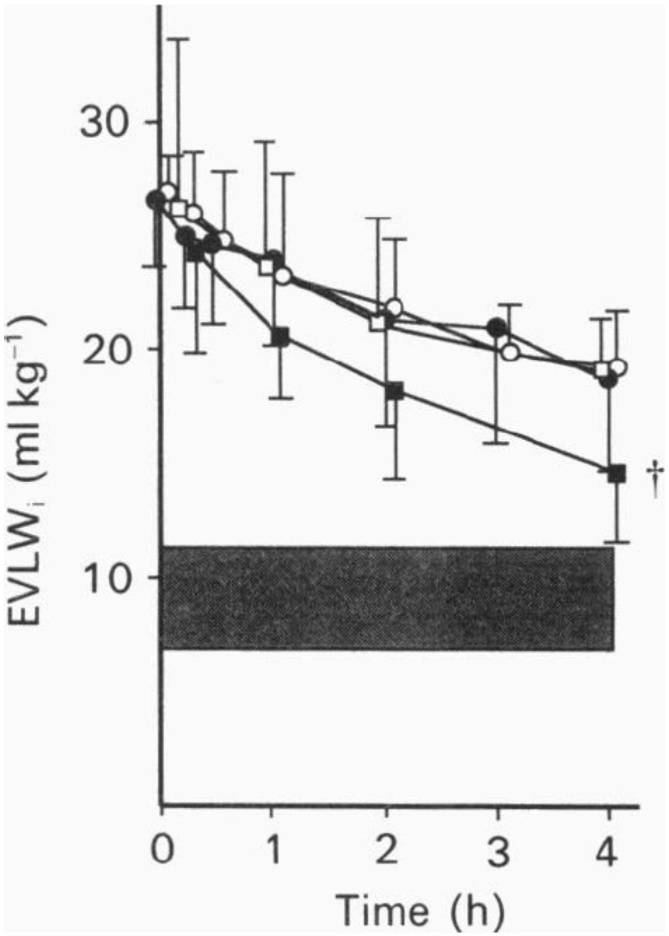
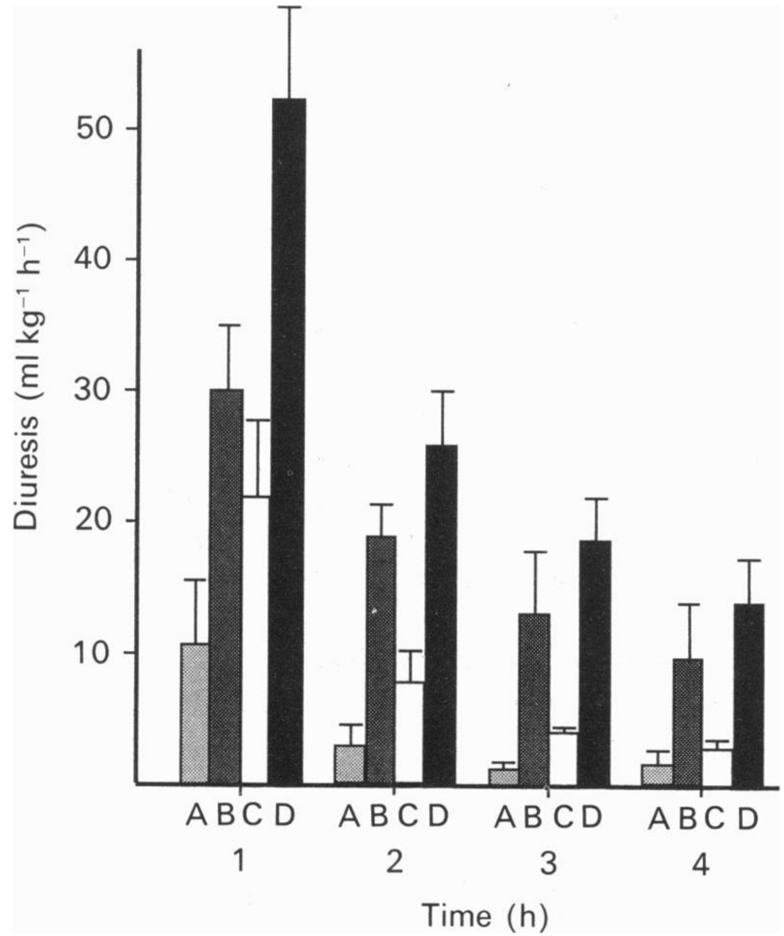


Fig. 2. Colloid oncotic pressure (COP; *A*) and serum osmolarity (*B*). Baseline value indicated as a shaded area represents a pooled mean value ± S.D. ($n = 14$) and the remaining data are given as mean values ± S.D. within each group (no standard deviation is plotted in groups A and B). Group A (□) = control, $n = 2$; group B (■) = furosemide, $n = 2$; group C (○) = HHS, $n = 5$; group D (●) = HHS + furosemide, $n = 5$. * Significantly different from preceding value ($P < 0{\cdot}05$). † Significant difference between groups C and D ($P < 0{\cdot}05$).

Wickerts CJ, Berg B, Frostell C, et al. Influence of hypertonic-hyperoncotic solution and furosemide on canine hydrostatic pulmonary oedema resorption. J Physiol 1992; 458: 425-438

Effect of Diuresis on Lung Water





Wickerts CJ, Berg B, Frostell C, et al. Influence of hypertonic-hyperoncotic solution and furosemide on canine hydrostatic pulmonary oedema resorption. J Physiol 1992; 458: 425-438

Diuresis May Decrease Plasma Volume

- Study design
  - Prospective observational study
- Subjects
  - 18 patients with medically treated, compensated HF
  - 27 health volunteers
- Measurements
  - Plasma volume determined by ^{125}I-albumin
  - ECV determined by single-injection method of ^{51}Cr-EDTA
- Conclusions
  - …patients treated with high doses of loop-diuretics tended to have subnormal PV…

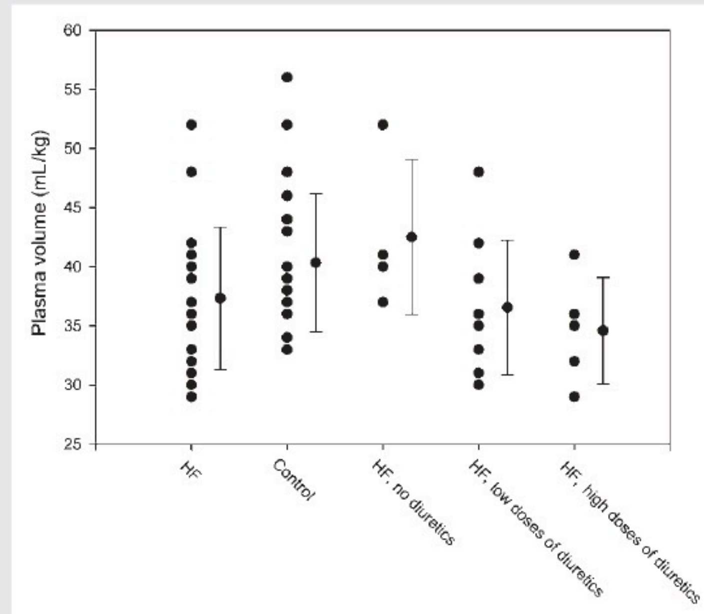


Figure 2 Plasma volume (mL/kg) in patients with heart failure, control subjects, and heart failure subgroups (no diuretics; low doses of diuretics corresponding to <100 mg furosemide daily; and high doses of diuretics corresponding to >100 mg furosemide daily).

Bonfils PK, Damgaard M, Taskiran M, et al. Impact of diuretic treatment and sodium intake on plasma volume in patients with compensated systolic heart failure. Eur J heart Fail 2010; 12: 995-1001

Hemodynamic Side Effects of Diuretics

- Intravascular volume depletion
- Hypotension
- Diminished cardiac output
- Renal dysfunction
  - Reduced glomerular filtration rate (GFR)
  - Increased creatinine

Cleland JGF, Coletta A, Witte K. Practical applications of intravenous diuretic therapy in decompensated heart failure. Am J Med 2006; 119: S26-S36

What Does Fluid Balance Mean?

The patient was placed on a fluid balance chart.

What Does Fluid Balance Mean?

- Inaccurate cumulative fluid balances very common
  - In 33% to 91.25% of all cases
- Significant errors in recorded cumulative fluid balances
  - ranging from -3606 ml to +2020 ml
  - mean absolute error 445 ± 668 ml
  - net difference in the opposite direction between recorded fluid balance and body weight change in 25% of cases
- Poor agreement between body weight changes and…
  - net cumulative fluid balance
  - adjusted cumulative fluid balance

Eastwood GM, Nsg GD. Evaluating the reliability of recorded fluid balance to approximate body weight change in patients undergoing cardiac surgery. Heart Lung 2006; 35: 27-33
Perren A, Markmann M, Merlani G, et al. Fluid balance in critically ill patients. Should we really rely on it? Minerva Anestesiol 2011; 77: 802-811

What Does Fluid Balance Mean?

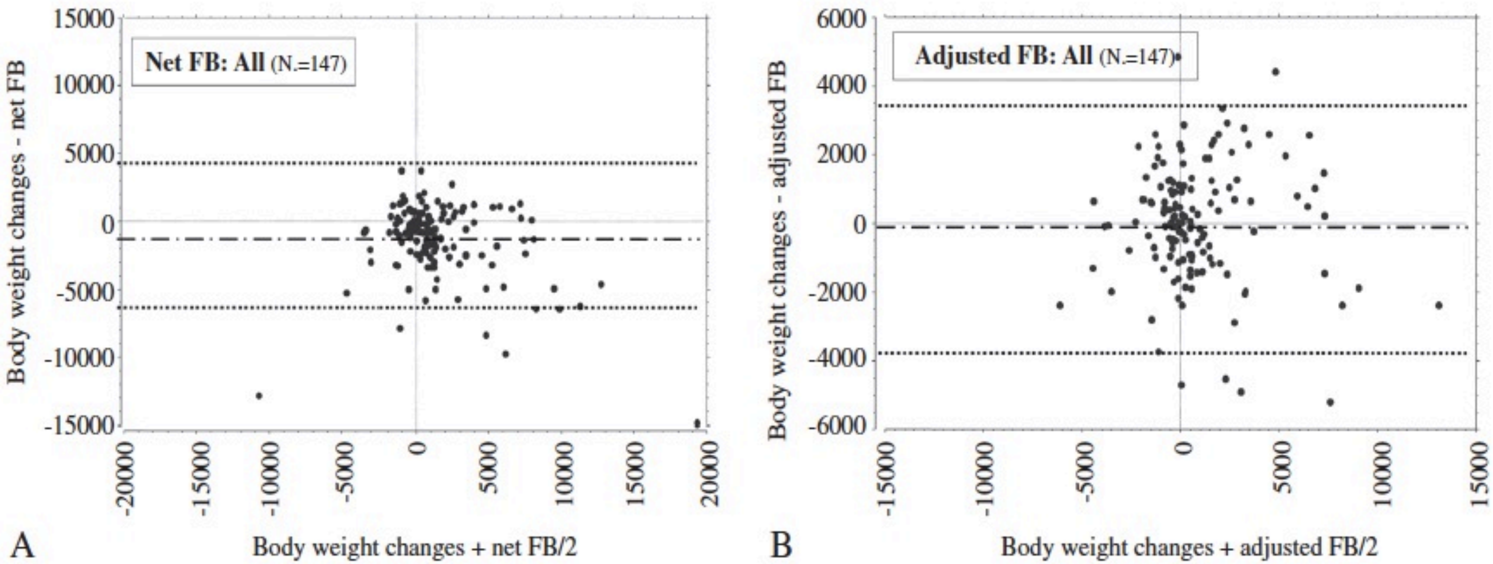


Figure 2.—Bland and Altman plot between the body weight changes and the cumulative net (Figure 2A) and adjusted (Figure 2B) fluid balances in all patients. FB: fluid balance; note the different scales on the y-axes.

Perren A, Markmann M, Merlani G, et al. Fluid balance in critically ill patients. Should we really rely on it? Minerva Anestesiol 2011; 77: 802-811

Fluid Balance: What Are We Talking About?

- We believe that clinical decision-making in the ICU setting should not be based on fluid balance. Daily body weight should be measured, and more objective techniques should be developed…
- There is a need for an accurate and specific definition of what clinicians and research authors mean by fluid balance…

Gonzalez F, Vincent F. The fluid balance in the critically ill patients: what are we talking about? Minerva Anestesiol 2011; 77: 766-767

Surrogate Markers

- Serum albumin
- Metabolic acidosis
- Platelet count
- Lactate level
- …

- Bedside monitor?!
- Fluid balance!

Take Home Message

- Fluid management important in the clinical management of critically ill patients
- Positive fluid balance and/or fluid overload often associated with poor clinical outcome
- Current evidence suggests fluid overload as a marker, rather than the cause, of poor prognosis
- Conservative fluid management strategy only applicable without evidence of hypovolemia and/or tissue hypoperfusion