Acute Kidney Injury and Fluid Management

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Case Presentation

65 year old man is admitted with multiple injuries following a motor vehicle accident.

On presentation to the Emergency Department he was initially hypotensive, with a blood pressure of 80/30 mm Hg and a hemoglobin of 10.1 g/dL.

He has multiple rib fractures with chest and abdominal wall contusion.

He undergoes a CT scan of the abdomen with intravenous contrast and is then taken to the OR for repair of a hepatic laceration and splenectomy for a splenic laceration.

Case (cont.)

BP: 130/80 on no pressors HR: 112

HEENT: Endotracheal tube in place

Lungs: Mechanically ventilated with decreased breath sounds over the left anterior lung fields

Cardiac: S_1S_2 nl, w/o gallop or murmur

Abdomen: Obese, distended with intact midline incision

Extremities: Left leg casted; extremities warm with strong pulses. 1+ flank edema

Neurologic: Sedated

Case (cont.)

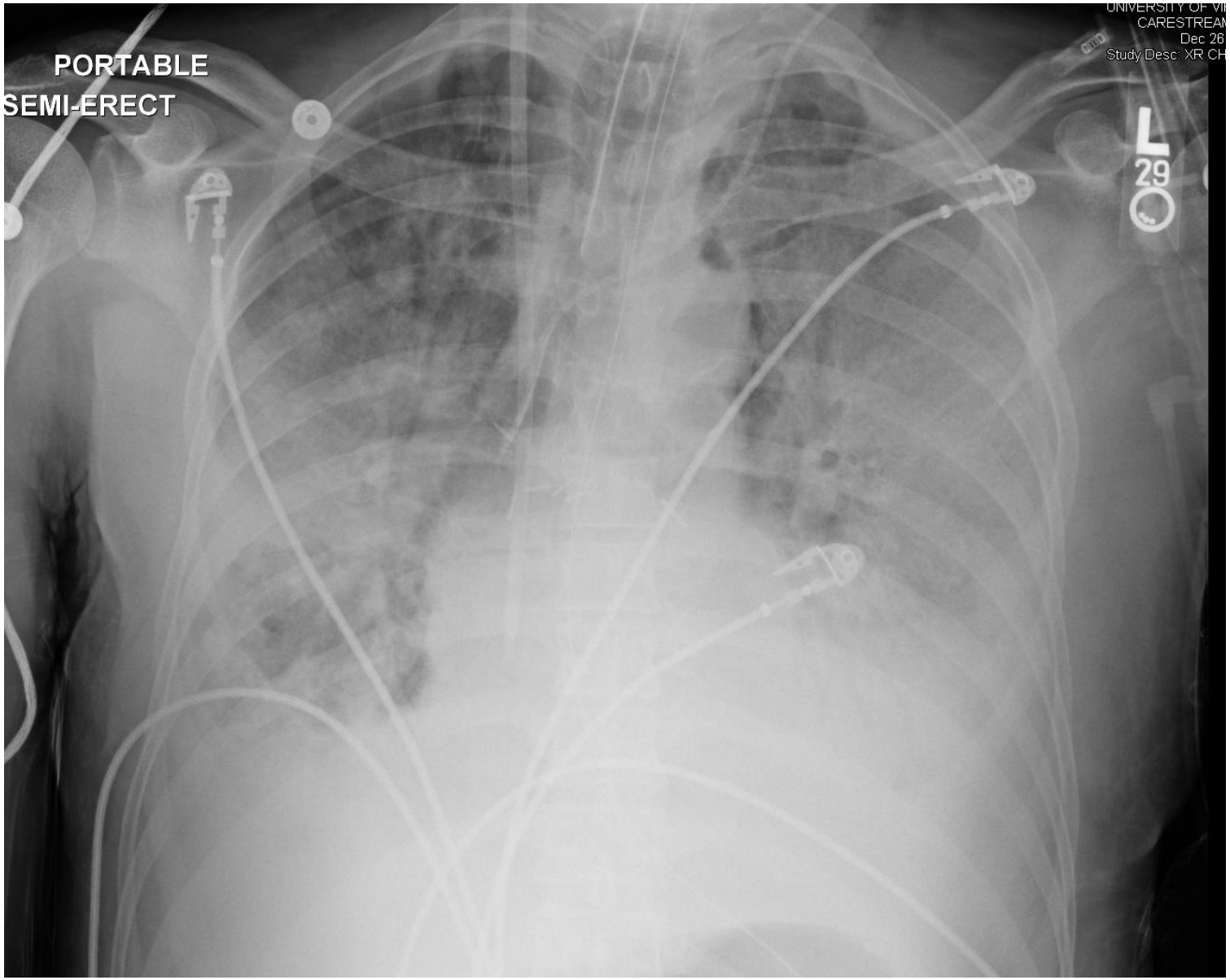
BUN:	28 mg/dL	Hgb:	9.7 g/dL
Creatinine:	1.8 mg/dL	Plt:	248,000/mm^3
Na:	137 mmol/L		
K:	5.3 mmol/L		
Cl:	105 mmol/L	CPK	1057 U/L
tCO_2:	21 mmol/L		

Urinalysis:

pH 5.5; S.G 1.030; 4+ blood; 1+ protein

microscopic: TNTC RBC's

Urine Sodium: < 10 mmol/L


PORTABLE
SEMI-ERECT
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29

Case (cont.)

Renal ultrasound

- Left kidney 12.3 cm
- Right kidney 11.9 cm
- No hydronephrosis
- Catheter balloon seen in bladder
- Small left retroperitoneal hematoma
- Large volume of ascites noted

Case (cont.)

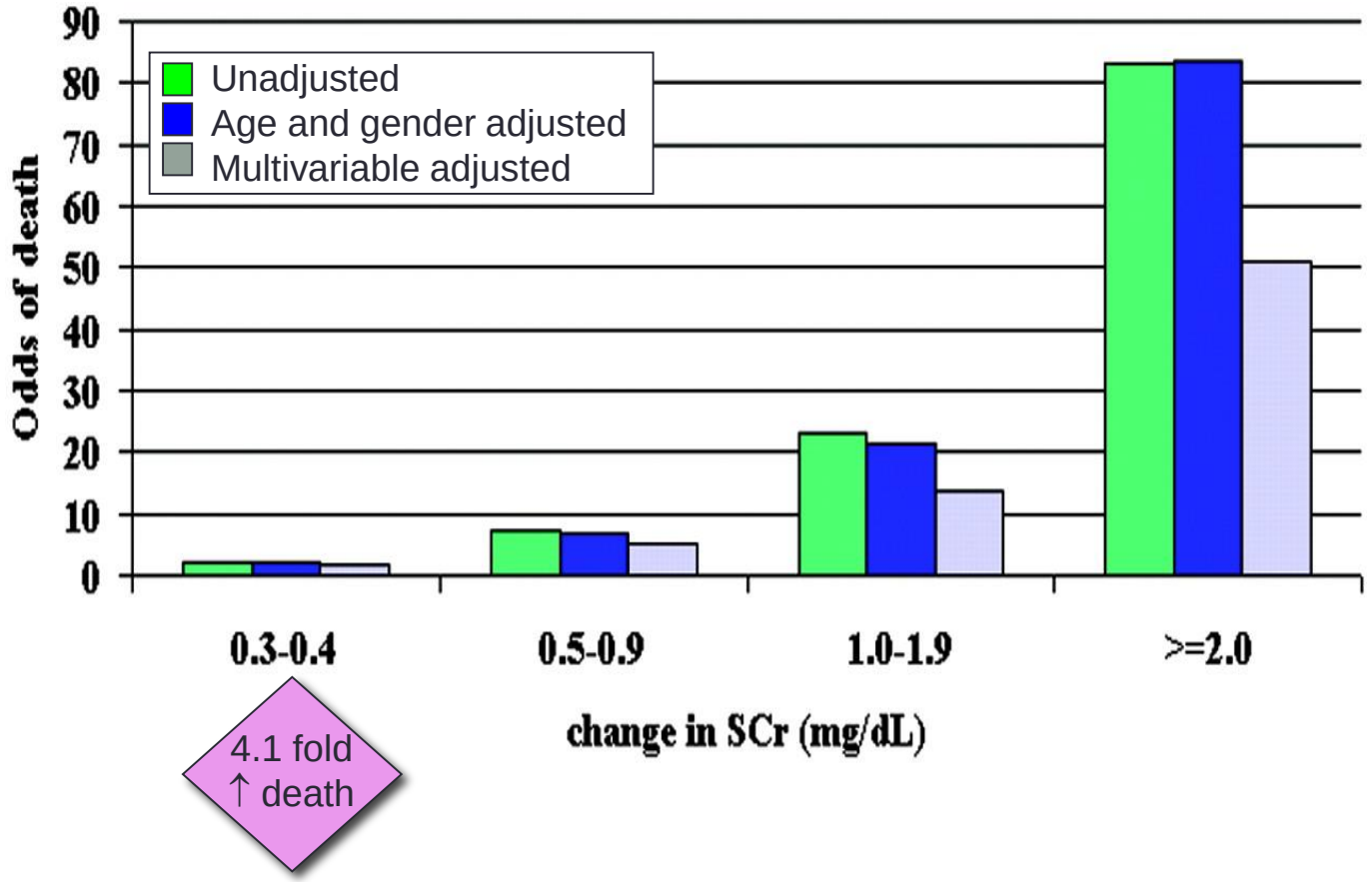
In the ICU, after transfusion of 4 units of packed red blood cells, multiple units of FFP and resuscitation with > 20 liters of fluid (HES and crystalloid), his blood pressure is 130/80 mm Hg on no pressor agents. His urine output is initially 5-10 mL/hour, however he becomes anuric 12 hours after ICU admission.

Hospital Course

- Bladder pressure was determined to be 27 mm hg, and surgical decompression was performed with urine output improving.
- Developed fever, sepsis with initiation of vancomycin, gentamicin and flagyl.
- He was anuric, creatinine now was 3.2 mg/dl and urinalysis showed numerous granular casts.
- Persistent hypotension requiring pressors and CRRT; suffered numerous complications, DIC, requiring blood products, pneumonia.
- Palliative care was consulted and along with family members the decision was made to withdraw care.

Small Increase in Serum Creatinine is Associated with Increase in Death

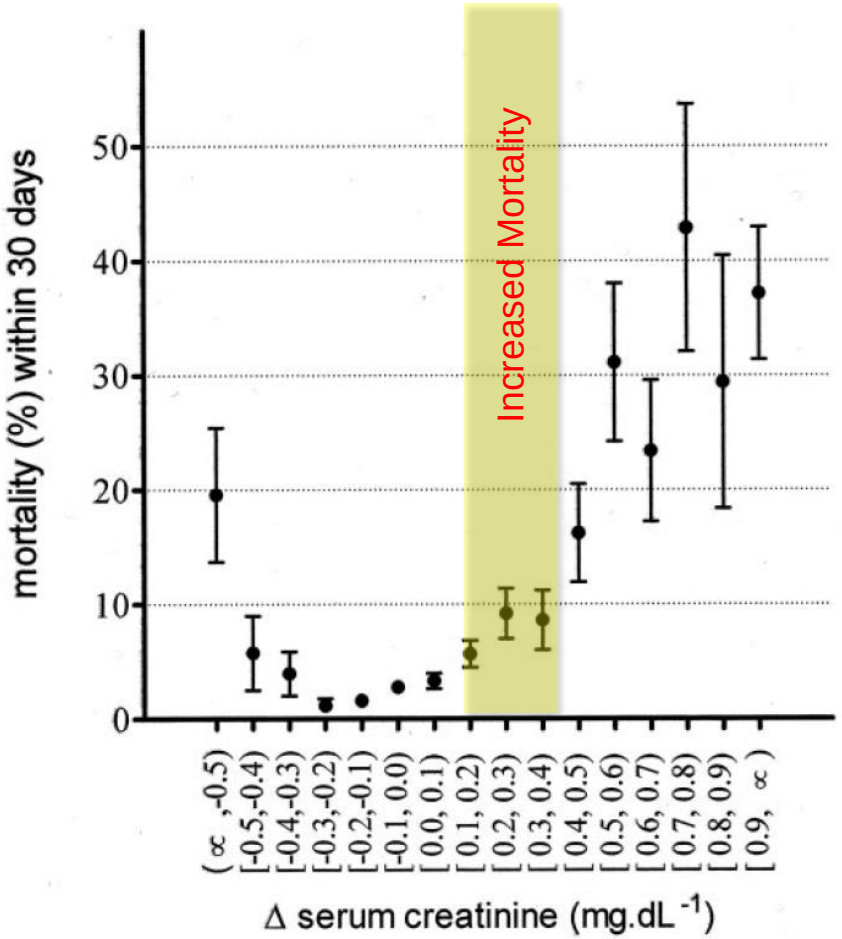
- There are few studies which have examined the effect of small changes in creatinine mortality
- Single academic medical center
  - Survey >19,000 hospital admissions
  - Subset with more than 1 creatinine was analyzed
  - Endpoint-death
- Result: Graded impact of death with increase in severity of AKI
  - Modest ↑Scr of 0.3 mg/dl increase was associated with 4.1 fold ↑ death.



G. M. Chertow et al. JASN 16:3365, 2005

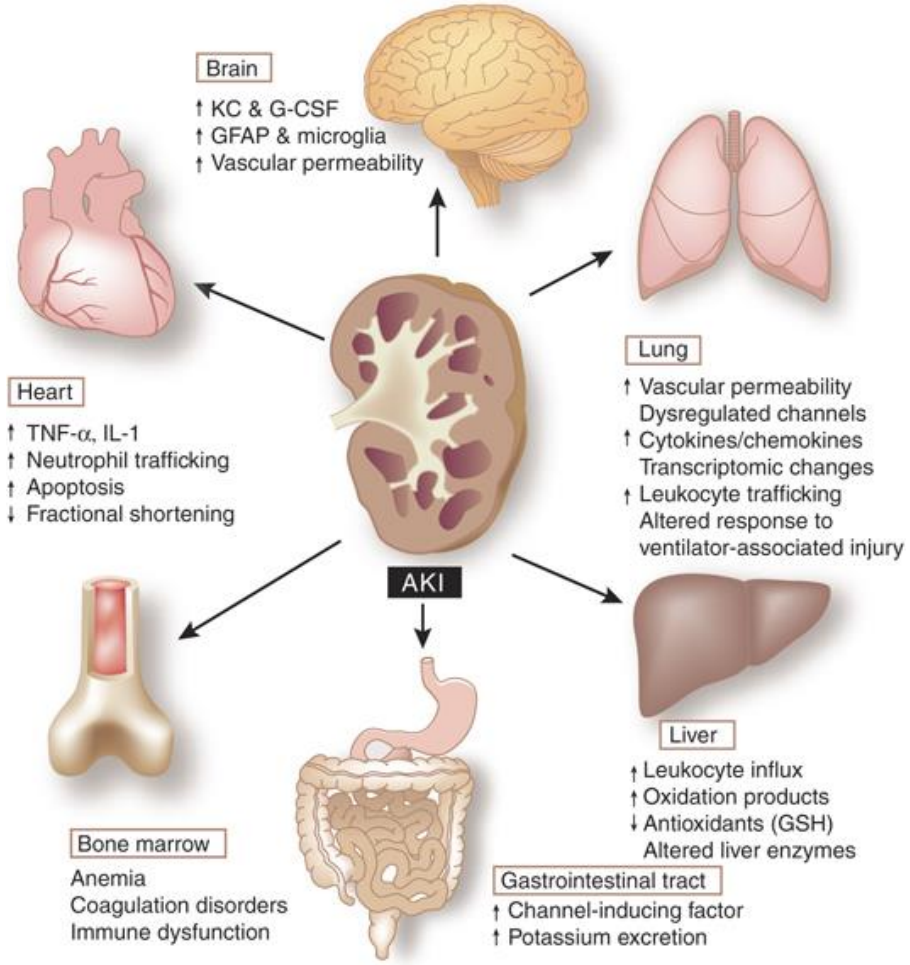
Minimal Changes of Serum Creatinine Predict Prognosis in Patients after Cardiothoracic Surgery

- Long ischemic times or dose of nephrotoxins lead to proportional increase in kidney injury
- Epidemiological studies demonstrate that even mild AKI not requiring dialysis or interventions is associated with significant increased mortality.
- Likely represents a summation of systemic effects of AKI.

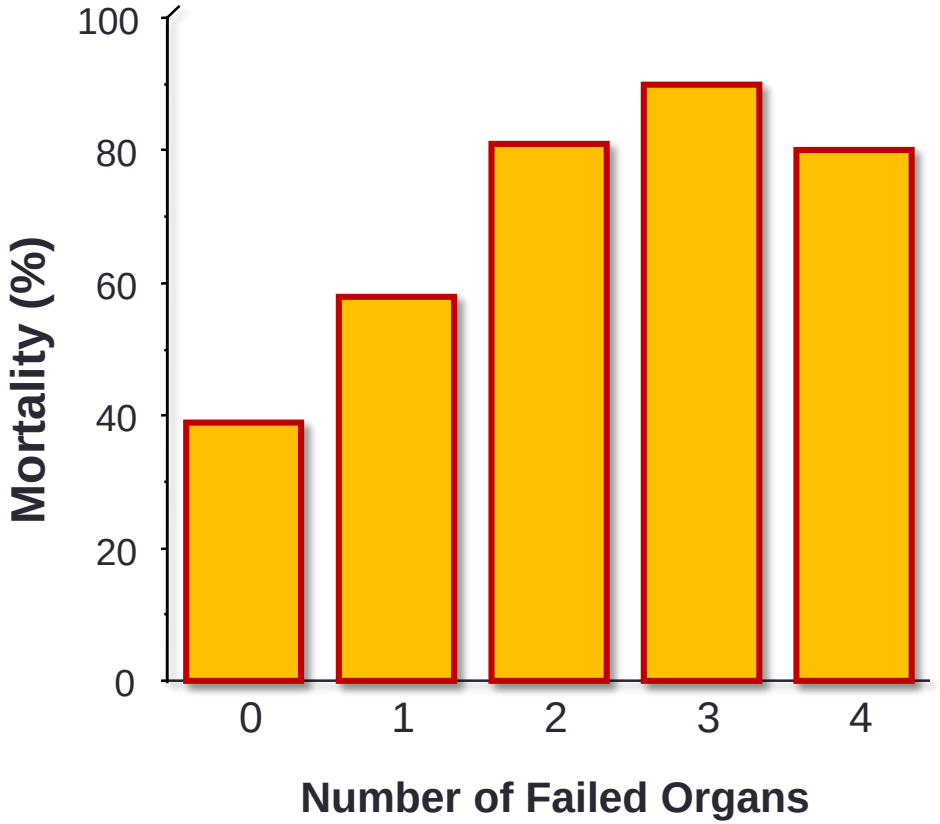


A. Lassnigg et al. JASN 15:1597-1605, 2004

AKI Leads to Distant Organ Dysfunction

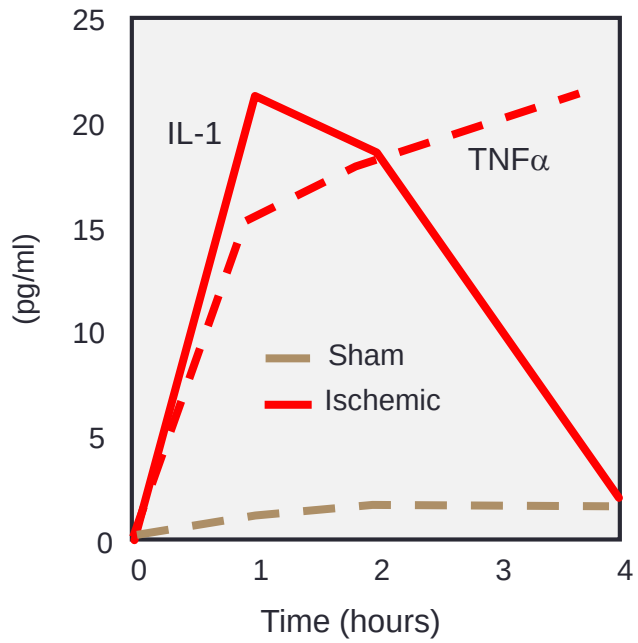


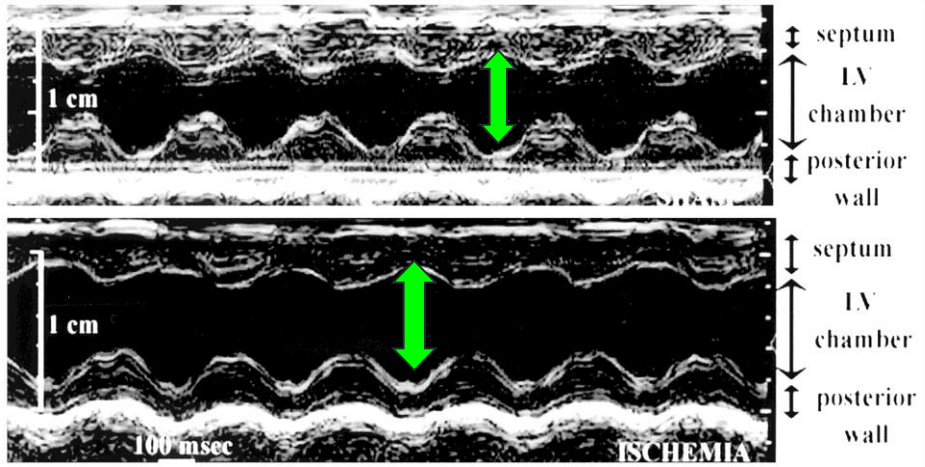
P Scheel, M. Liu and H. Rabb, Kidney Int 74:849, 2008



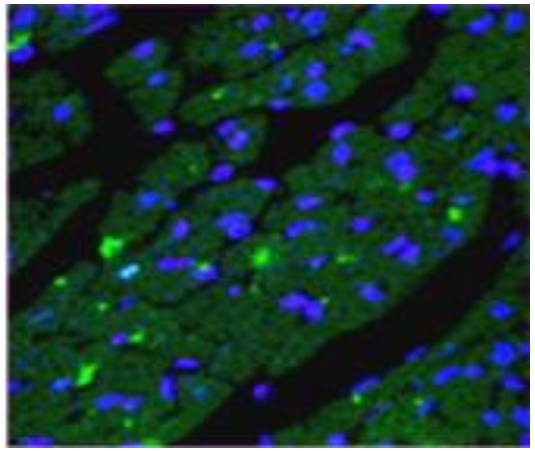
Redrawn from R. A. Star, Kidney Int. 54:1817,1998

IL- 1and TNF increase after renal ischemia and induce TNF-mediated cardiac apoptosis and impaired contractility

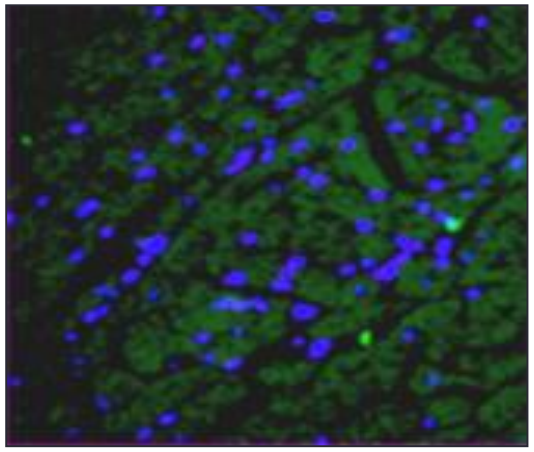




ischemia/ reperfusion



anti-TNF/ ischemia/ reperfusion

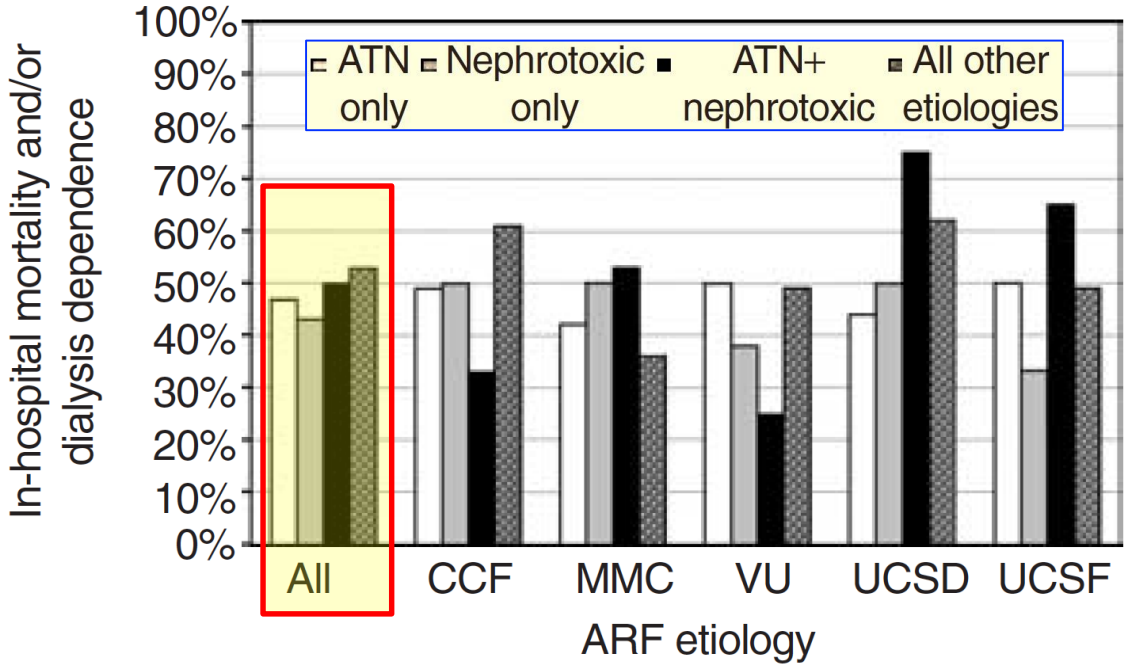


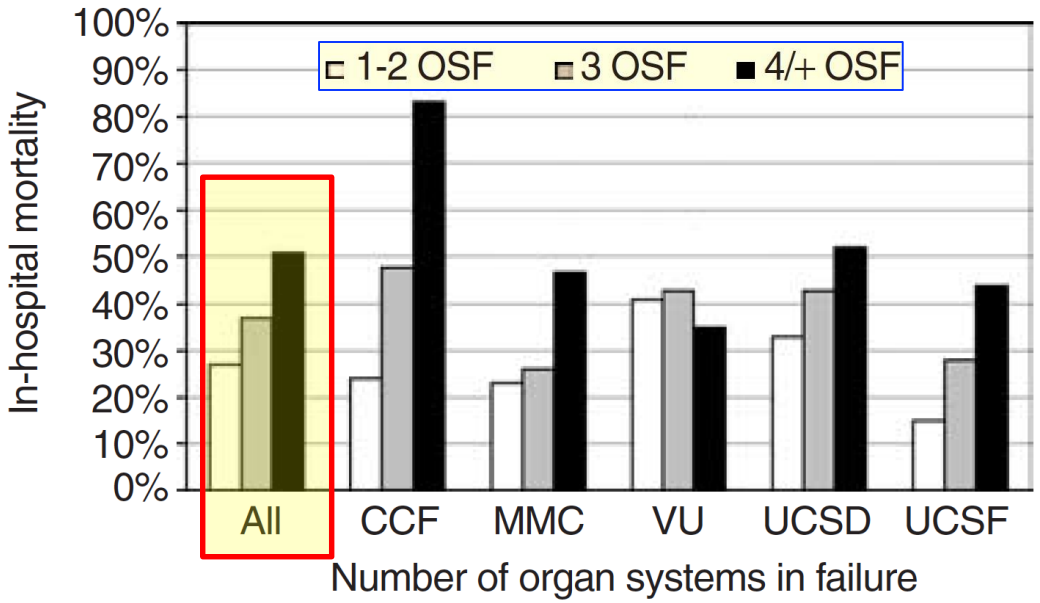
Kelly, K.J, et al. J Clin Invest, 97: 1056-1063, 1996

Organ System Failure in AKI

AKI is a Systemic Disease

- PICARD study-618 patients/396 with AKI requiring dialysis
  - Prospective cohort
  - 5 teaching U.S. hospitals
  - Between 1999 and 2001
- Acute renal failure was accompanied by
  - extrarenal organ system failure in most patients
  - Organ system failure occurred in even those who did not require dialysis.
    - 64% patients required dialysis.





R. Mehta Kidney Int (2004) 1613-17621

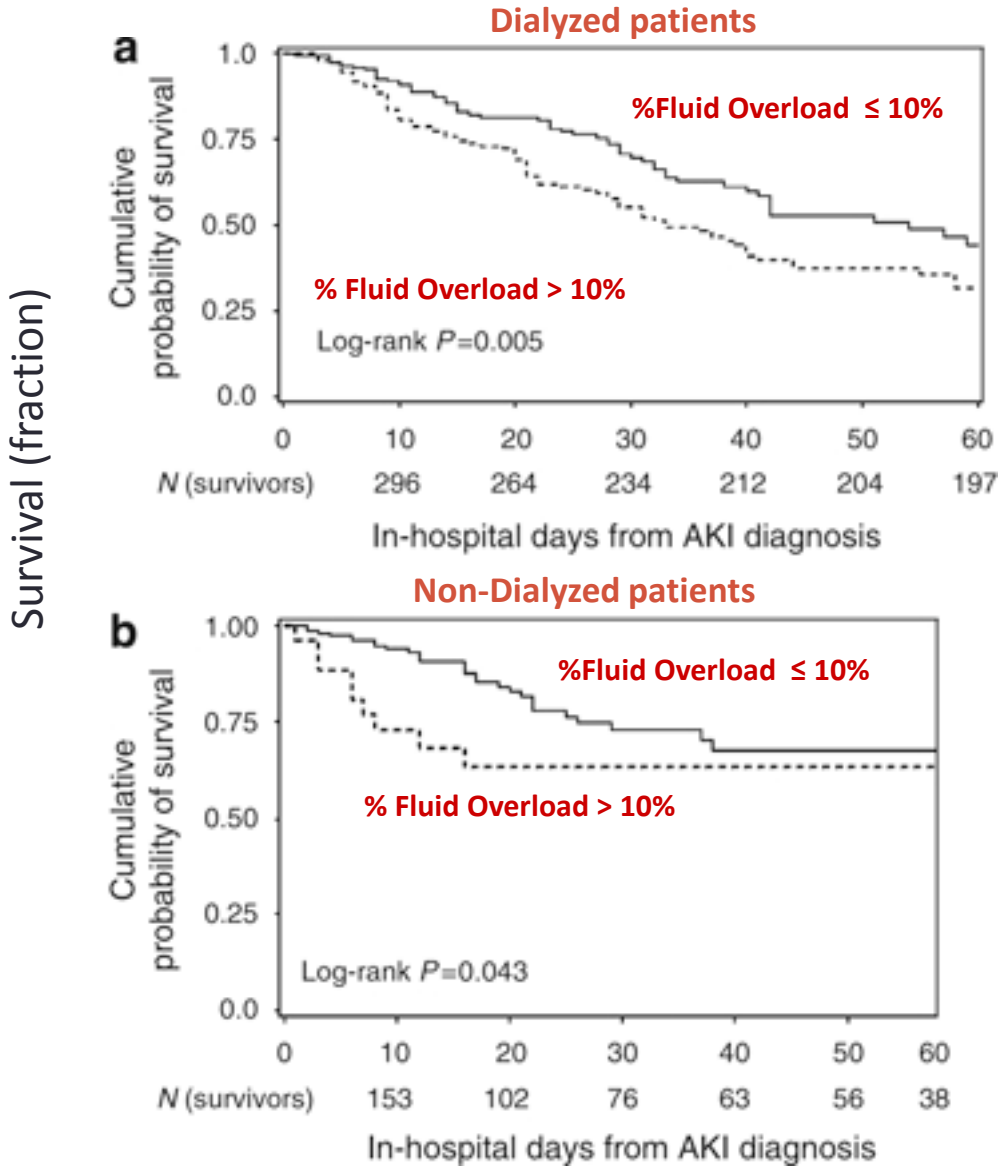
Fluid Overload and Poor Outcomes

Fluid overload- poor outcomes in AKI patients

- 396 patients with AKI requiring dialysis
- PICARD study
  - Prospective cohort
  - 5 teaching U.S. hospitals
  - Between 1999 and 2001

MORTALITY-after adjusting for APACHE III

- Dialyzed patients: a 2.07 fold increase in the odds of death (95% CI 1.27-3.37)
- Non-dialyzed patients: 3.14 fold increase in the odds of death (95% CI 1.18–8.33).



J. Bouchard et al. Kidney Int. 76:422-7, 2009 (Aug)

WHY IS FLUID OVERLOAD ASSOCIATED WTH INCREASE IN MORTALITY?

Volume overload delays recognition of AKI and may lead to an increase in mortality

Program to Improve Care in Acute Kidney Disease (PICARD)

- 253 patients in PICARD database (n=618) with consecutive increase in serum Cr over 3-7 days
- Serum creatinine values were adjusted according to the cumulative daily fluid balance using the formula:
  - *Cr adjusted = serum Cr x correction factor*[1]

[1]Correction factor = [hospital admit wt(kg) x 0.6 + Σ (daily fluid balance)]/hospital admit wt x 0.6

E. Macedo…R. Mehta Crit Care 2010:14:R82

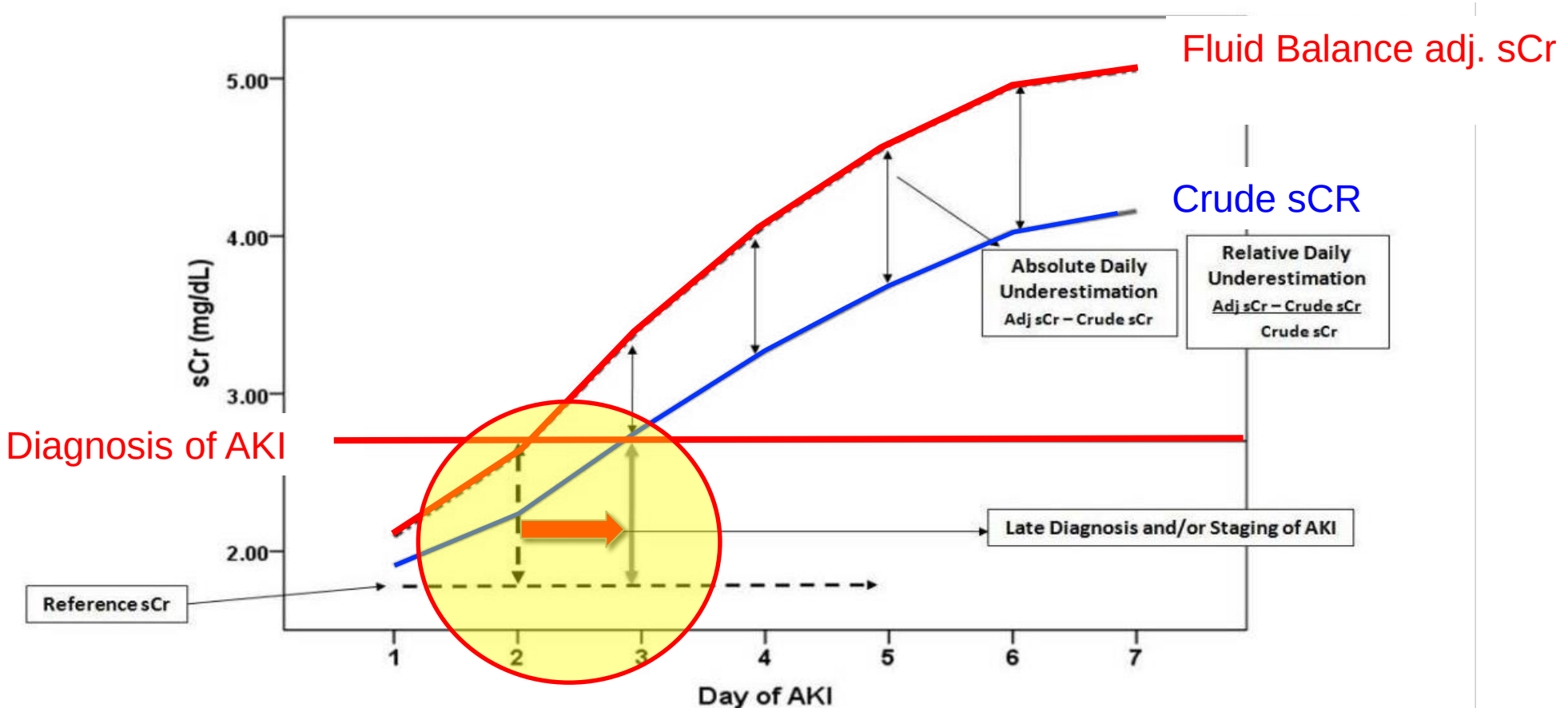
Volume overload delays recognition of AKI

Daily Cumulative Fluid Balance and SCr (adjusted and non-adjusted)

	day 0	day 1	day 2	day 3	day 4	day 5	day 6
cumulative FB - Liters (median)		2.7	3.7	4.95	5.6	6	6.5
IQR 25%-75%		0.50 - 6.20	1.15 - 8.60	1.72 - 10.30	2.50 - 12.00	1.90 - 13.1	1.07 - 11.32
SCr non-adjusted	1.6	2.1	2.8	3.3	3.8	3.85	3.9
SCr - FB adjusted	1.69	2.24	3	3.79	4.29	4.44	4.55
IQR 25% - 75%	1.20 - 2.32	1.61 - 3.06	2.31 - 4.24	2.86 - 5.23	3.23 - 6.29	3.44 - 6.31	3.42 - 6.68

E. Macedo…R. Mehta Crit Care 2010:14:R82

Volume overload delays recognition of AKI



E. Macedo…R. Mehta Crit Care 2010:14:R82

AKI, Fluid Overload and GI Tract

- 152 pts undergoing elective intraabdominal surgery.
  - Liberal (liberal protocol group [LPG]*
  - Restrictive (restrictive protocol group [RPG]*
- Primary endpoint: death or complications.
- Secondary endpoints: 1) initial passage of flatus and feces, 2) duration of hospital stay, and 3) changes in body weight, hematocrit, and albumin serum concentration in the first 3 postoperative days
- Results, RPG associated:
  - Lower Complications ($P = 0.046$)
  - Earlier passage of flatus and feces, ($P < 0.001$ and $P < 0.001$)
  - Postoperative hospital stay was significantly shorter ($P = 0.01$).
- Intraabdominal surgery-case for intraoperative use of restrictive fluid management.

*Liberal (liberal protocol group [LPG], n = 75; bolus of 10 ml/kg followed by 12 ml/kg/h)
*Restrictive Group: n = 77; 4 ml/kg/h) amounts of LR

V. Nisanevich et al. Anesthesiology 103(1), July 2005, pp 25-32

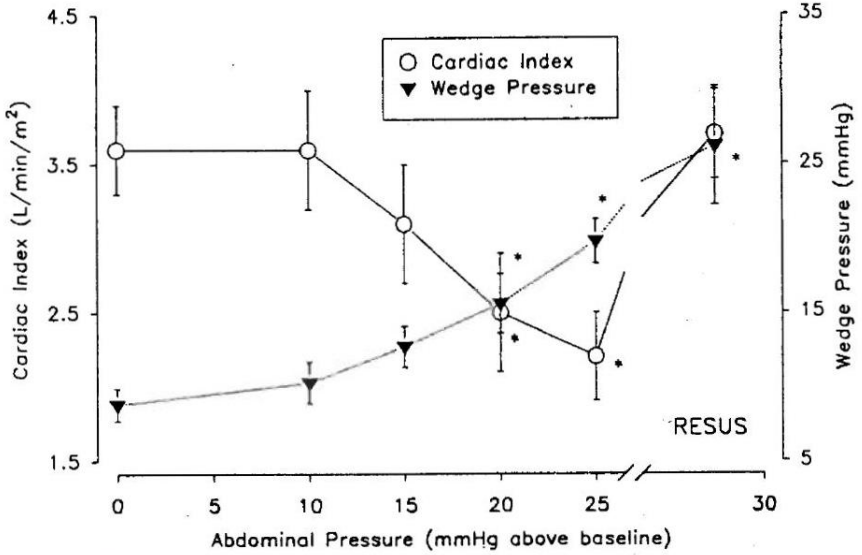
AKI, Fluid Overload and GI Tract

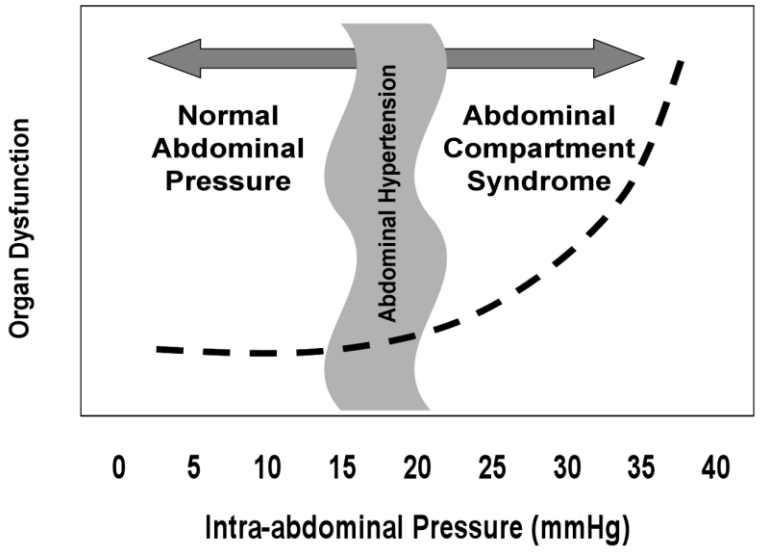
- Bowel edema
- Poor wound healing
- Poor drug absorption
- Poor nutrition
- Aggravates renal function
- Mesenteric vein compression
- Bowel ischemia
- Bacterial translocation

Abdominal pressure:	Total Prevalence	MICU prevalence	SICU prevalence
IAP > 12	58.8%	54.4%	65%
IAP > 15	28.9%	29.8%	27.5%
IAP > 20 plus organ failure	8.2%	10.5%	5.0%

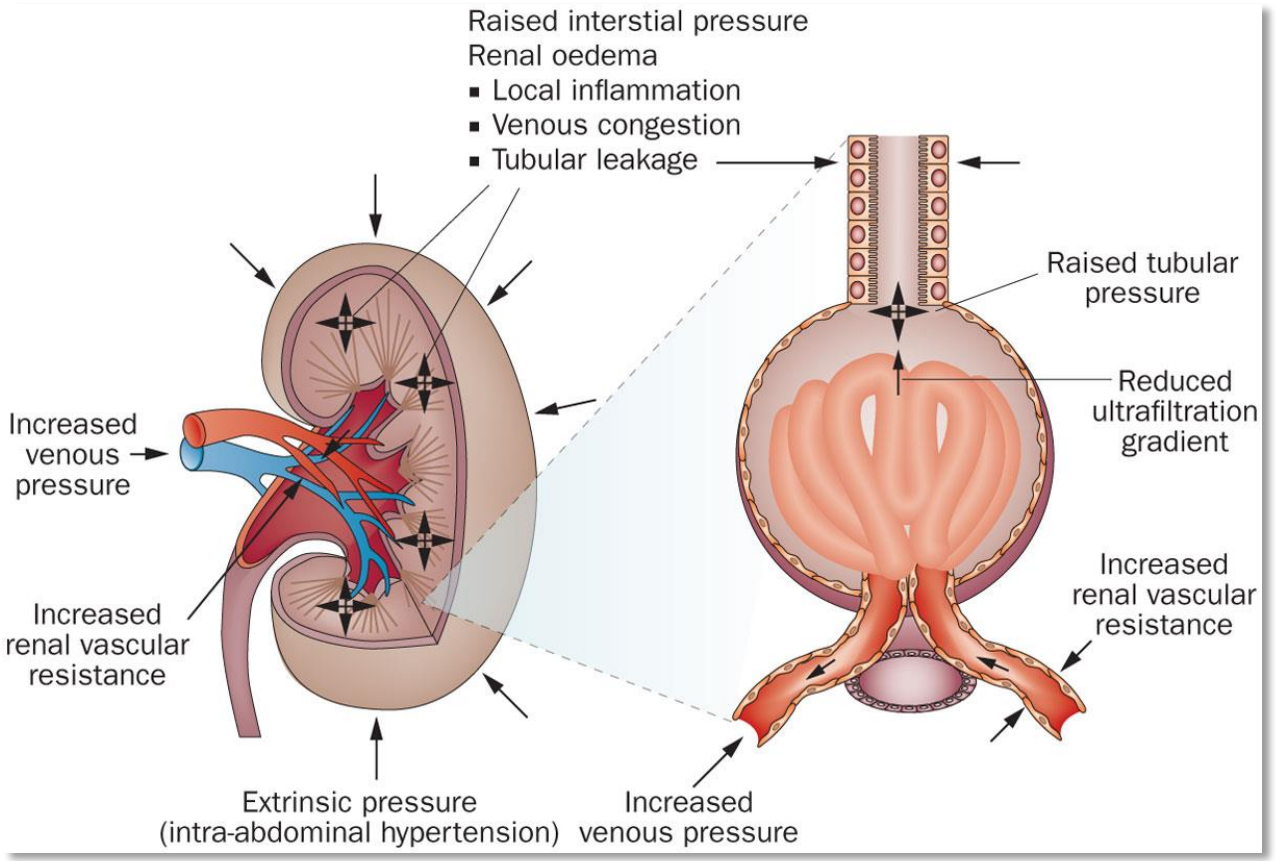
Ridings, et al 1995

Hemodynamic effect of IAH





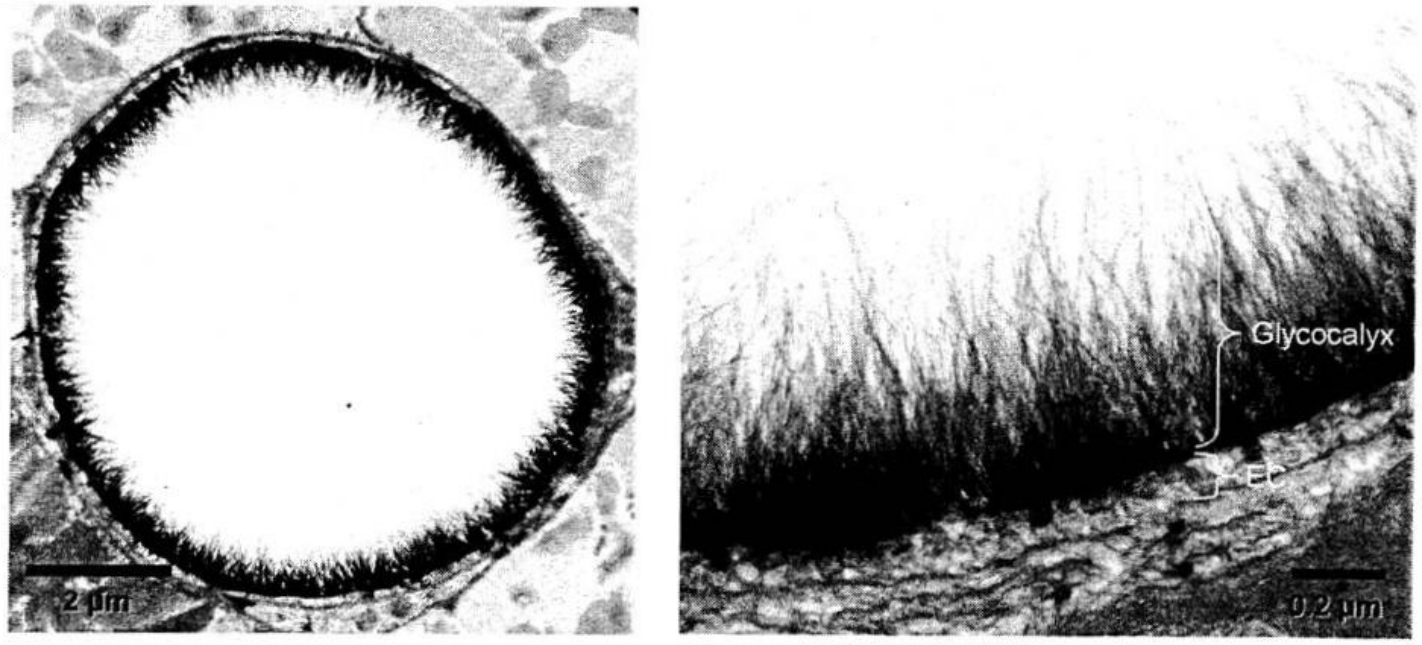
Fluid overload and interstitial edema can contribute to the maintenance of AKI

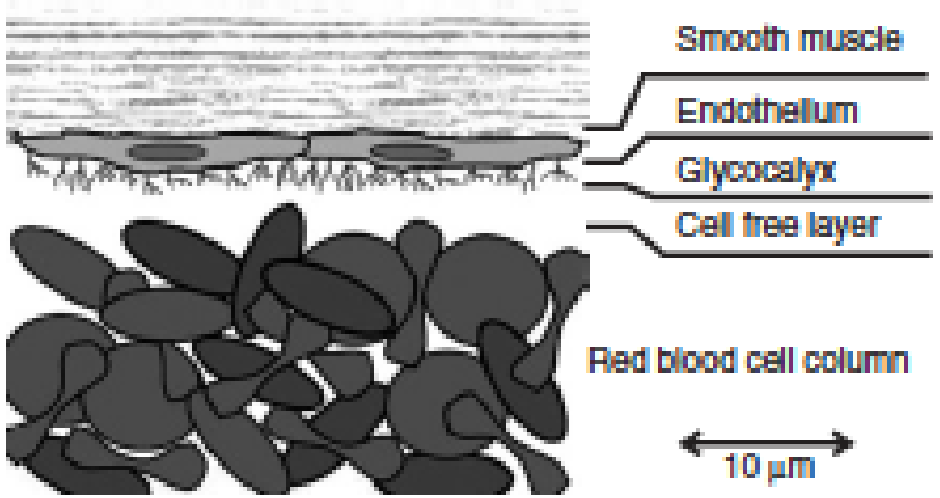


Prowle, J. R. *et al.* (2013) *Nat. Rev. Nephrol.* 10, 37–47 (2014)

$SNGFR = k \times S (P_{GC} - P_t - \pi_{GC})$

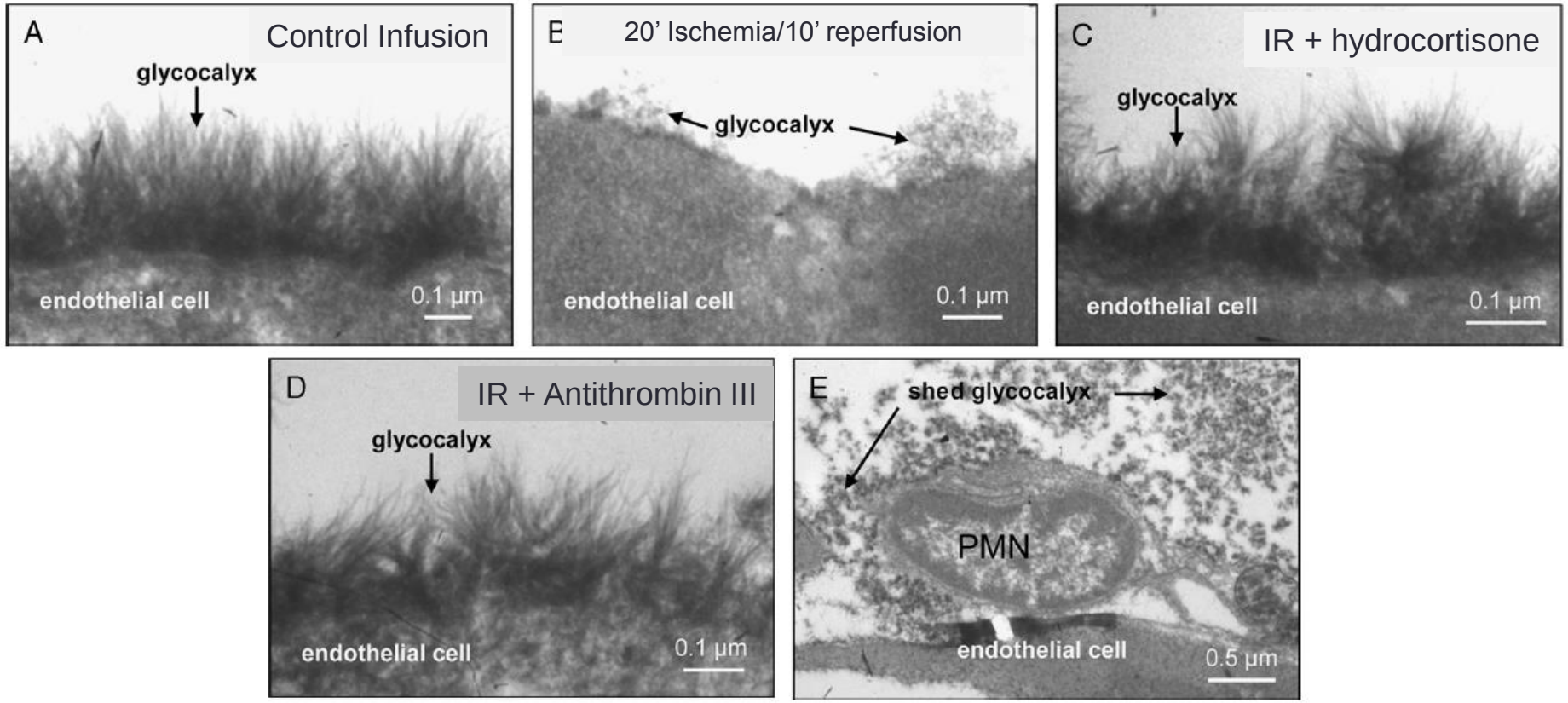
Glycocalyx





B.M. van den Berg et al. Pharmacological Reports 58: suppl 75-80, 2006

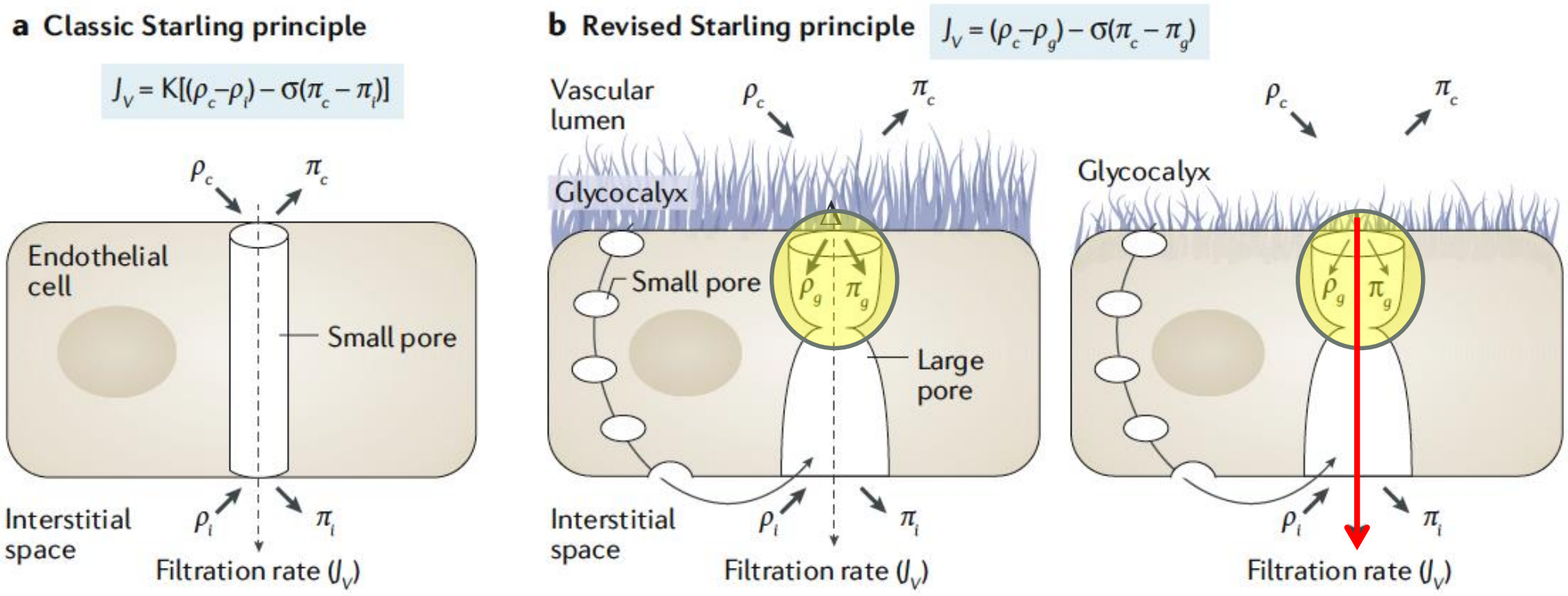
Glycocalyx Degradation after IRI



perfusion (group G). B, Degradation to a rudimentary glycocalyx after 20 min of warm ischemia and 10 min of reperfusion (group A). C and D, Mostly intact glycocalyx after pretreatment with hydrocortisone (10 µg/mL perfusate, C) or antithrombin III (1 U/mL perfusate, D) for 15 min during equilibration, respectively, followed by 20 min of warm ischemia and 10 min of reperfusion (groups B and C, respectively). However, the glycocalyx appears slightly less homogeneous in the pretreated hearts. E, Adherent polymorphonuclear granulocyte (PMN) surrounded by shed fragments of glycocalyx.

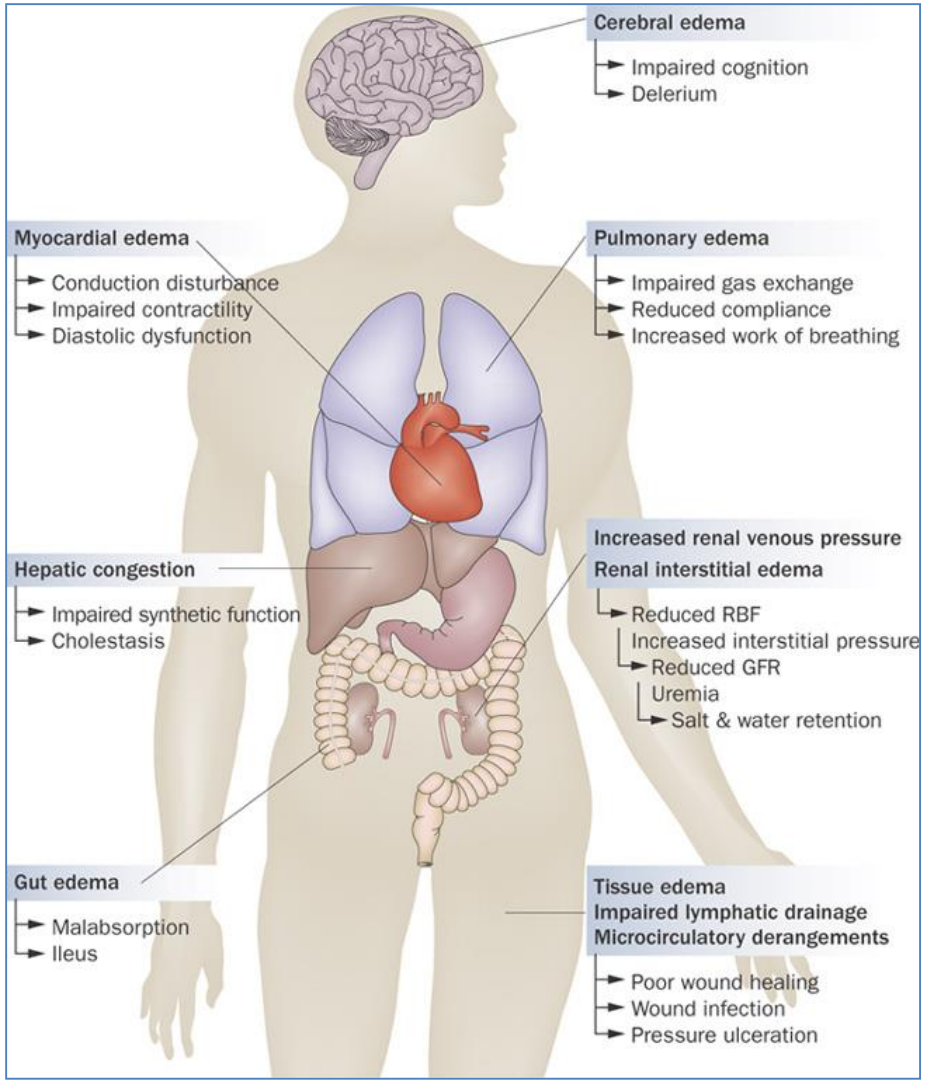
D Chappell et al. Shock 34:133, 2010

The Starling principle of fluid transport across capillary membranes



S Finfer, J Myburgh and R Bellomo Nat Rev Nephrol 2018

Fluid Overload and Organ Dysfunction



Prowle, J. R. et al. Nat. Rev. Nephrol.;6(2):107-15

HOW MUCH FLUID SHOULD BE GIVEN?

The History of Invention of IV Fluid Therapy

Thomas Latta first used IV saline in the 1832 cholera epidemic

Cholera hit Scotland in 1832, blood letting was a staple treatment. Reduced amount of water in the blood of patients. Latta attempted rectal delivery of salt solution without success. In the Lancet published June 2, 1832, Latta described injecting salty water into the basilic vein in increasingly large volumes in patients with terminal cholera, with remarkable results. The recipe: 58 mEq of sodium, 49 mEq of chloride and 9 mEq of hydrogen carbonate.

"… she began to breathe less laboriously, soon the sharpened features, and sunken eyes, … began to glow with returning animation; the pulse, which had been long ceased, returned to the wrist; at first small and quick, by degrees it became more and more distinct, fuller, slower and firmer, and in the short space of half an hour, when six pints had been injected, she expressed in a firm voice that she was free from all uneasiness … ."

Despite these early reports, it did not enter routine practice for another 100 years.

T. Latta, Lancet 18:274-80, 1832

The New England Journal of Medicine

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

- Severe sepsis or septic shock to receive either six hours of early-directed therapy or standard therapy before admission to the intensive care unit.
- 130 – EGT and 133 – standard Tx
- Physiologic end-points: MAP > 65 mm Hg, CVP > 8-12 mm Hg; Urine output (> 0.5 ml/kg/hour); Cardiac output; ScvO2 (> 70%)
- In-hospital mortality was 30.5% for EGT and 46.5% for the group assigned to standard therapy (P=0.009).
- EGT Tx –improved
  - central venous oxygen saturation
  - lactate concentration
  - base deficit
  - pH (7.40±0.12 vs. 7.36±0.12)
  - mean APACHE II

Rivers et al N Engl J Med 345: 1368, 2001

Goal-directed Resuscitation in Early Septic Shock

ARISE Investigators

- Multcenter study of 1600 pts; 796 were assigned to the EGDT group and 804 to the usual-care group. Randomly assigned patients in ED with early septic shock to receive either EGDT or usual care.
- The primary outcome was all-cause mortality within 90 days after randomization.
- Patients in the EGDT group received a larger volume of intravenous fluids in the first 6 hours (1964 vs 1713 ml) and vasopressor infusions (66.6% vs. 57.8%), red-cell transfusions (13.6% vs. 7.0%), and dobutamine (15.4% vs. 2.6%) (P<0.001).
- At 90 days after randomization death rate of 18.6% and 18.8% (P=0.90).
- There was no significant difference in survival time, in-hospital mortality, duration of organ support, or length of hospital stay.
- CONCLUSIONS: In early septic shock, EGDT did not reduce all-cause mortality at 90 days

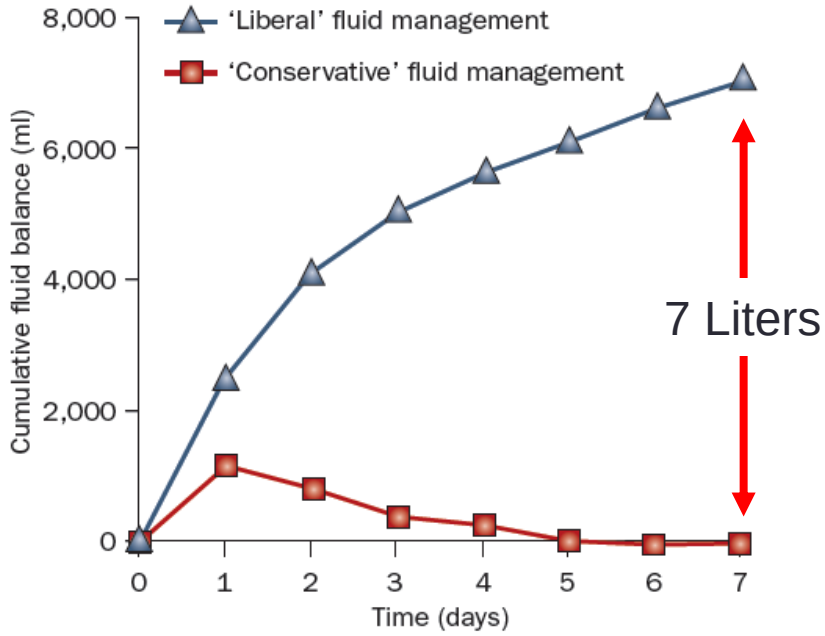
N Eng J Med 371: 1496-1506, 2014

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Comparison of Two Fluid-Management Strategies in Acute Lung Injury

The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network*



- Conservative and a liberal fluid management for 7 days in 1000 pts with ALI.
- Primary end point was death at 60 days.
- Secondary end points: # of ventilator-free days, organ-failure–free days and measures of lung physiology.
- The mean cumulative fluid balance during the first 7 days was –136 ml in the conservative-strategy group and ~7L in the liberal-strategy group (P<0.001).
- No difference in mortality at 60 days
- Conservative strategy of fluid management improved lung function and shortened duration of mechanical ventilation and intensive care
- Trend for reduced need for renal replacement therapy (10% restrictive v. 14% for liberal, p = 0.06) despite higher BUN and creatinine in the restrictive group.

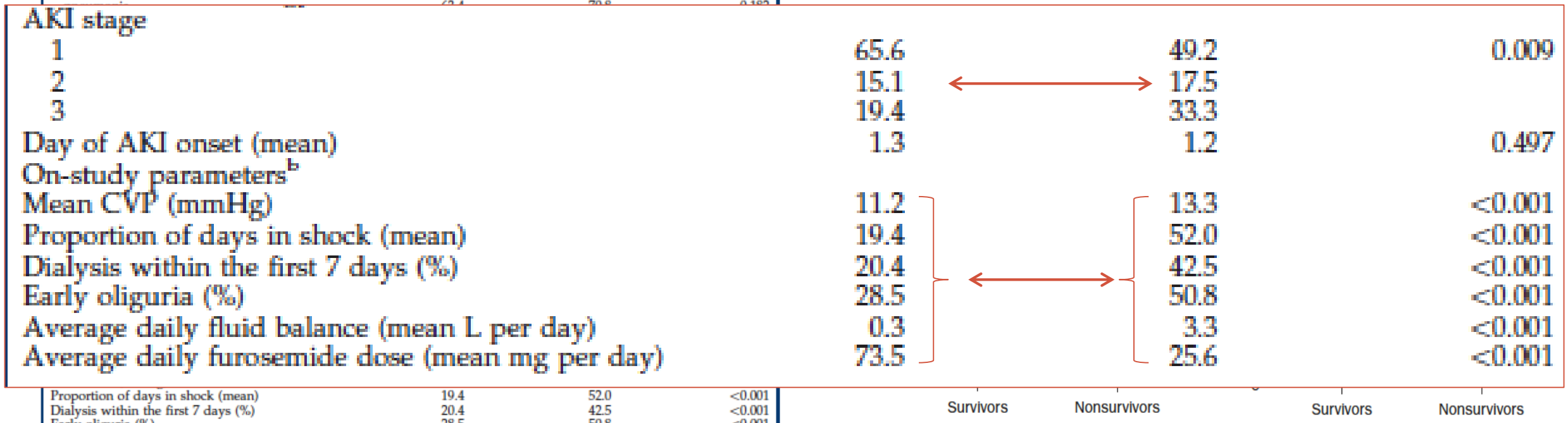
N Engl J Med. 354:2564-75, 2006.
Prowle, J. R. et al. Nat. Rev. Nephrol. 6, 107–115,2010;

Survivors and Nonsurvivors in Patients with AKI - FACTT Trial n=306

Table 2. Variables associated with 60-day survival among FACTT participants with AKI

FACTT Participants with AKI	Survivors	Nonsurvivors	*P*
n (%)	186 (60.8)	120 (39.2)	
Female (%)	44.1	39.2	0.395
Race (%)			
white	59.7	54.2	0.634
black	26.9	30.8	
other	13.4	15.0	
Age (mean, years)	47.4	53.9	<0.001
Contributing etiology of ALI (%)[a]			
trauma	10.8	1.7	0.003
sepsis	45.7	59.2	0.021
multiple transfusions	3.8	4.2	0.859
aspiration	11.8	16.7	0.230
AKI stage			
1	65.6	49.2	0.009
2	15.1	17.5	
3	19.4	33.3	
Day of AKI onset (mean)	1.3	1.2	0.497
On-study parameters[b]			
Mean CVP (mmHg)	11.2	13.3	<0.001
Proportion of days in shock (mean)	19.4	52.0	<0.001
Dialysis within the first 7 days (%)	20.4	42.5	<0.001
Early oliguria (%)	28.5	50.8	<0.001
Average daily fluid balance (mean L per day)	0.3	3.3	<0.001
Average daily furosemide dose (mean mg per day)	73.5	25.6	<0.001

[a]Participants were assigned up to two contributing etiologies for their acute lung injury.
[b]All on-study parameters are shown over the entire protocolized period, including pre-AKI.



Data taken from Grams, M. E. *et al*. *Clin. J. Am. Soc. Nephrol.* doi:10.2215/CJN.08781010

Glassford, N. J. & Bellomo, R. *Nat. Rev. Nephrol.7:* 305-306, 2011

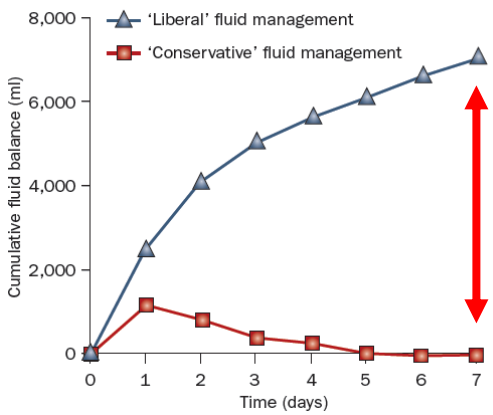
Conclusion: FACTT patients with AKI

A positive fluid balance after the development of AKI is associated with increased mortality, as well as progression to more severe grades of AKI and increased requirement for renal support. In addition, the data suggest that diuretics are, at least, safe to use during critical illness and may have a beneficial survival effect through the achievement of a more-negative fluid balance.

Glassford, N. J. & Bellomo, R. *Nat. Rev. Nephrol.7:* 305-306, 2011

Acute kidney injury in patients with acute lung injury: Impact of fluid accumulation on classification of acute kidney injury and associated outcomes*

Kathleen D. Liu, MD; B. Taylor Thompson, MD; Marek Ancukiewicz; Jay S. Steingrub, MD; Ivor S. Douglas, MD; Michael A. Matthay, MD; Patrick Wright, MD; Michael W. Peterson, MD; Peter Rock, MD; Robert C. Hyzy, MD; Antonio Anzueto, MD; Jonathon D. Truwit, MD, MBA; for the National Institutes of Health National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome Network



- Fluid accumulation may delay recognition of AKI because creatinine is diluted
- Negative fluid balance, creatinine may become relatively concentrated and patients may be more likely to meet criteria for AKI.
- Serum creatinine measurements should be adjusted for fluid balance
- After adjustment for increased fluid volume
  - Incidence of AKI was lower in the conservative group 58 vs 66% (P<0.007)
  - Mortality rate was lower in the conservative group 11 vs 31% (P<0.005)

Liu et al. Crit Care Med 39:2665, 2011

The NEW ENGLAND JOURNAL of MEDICINE

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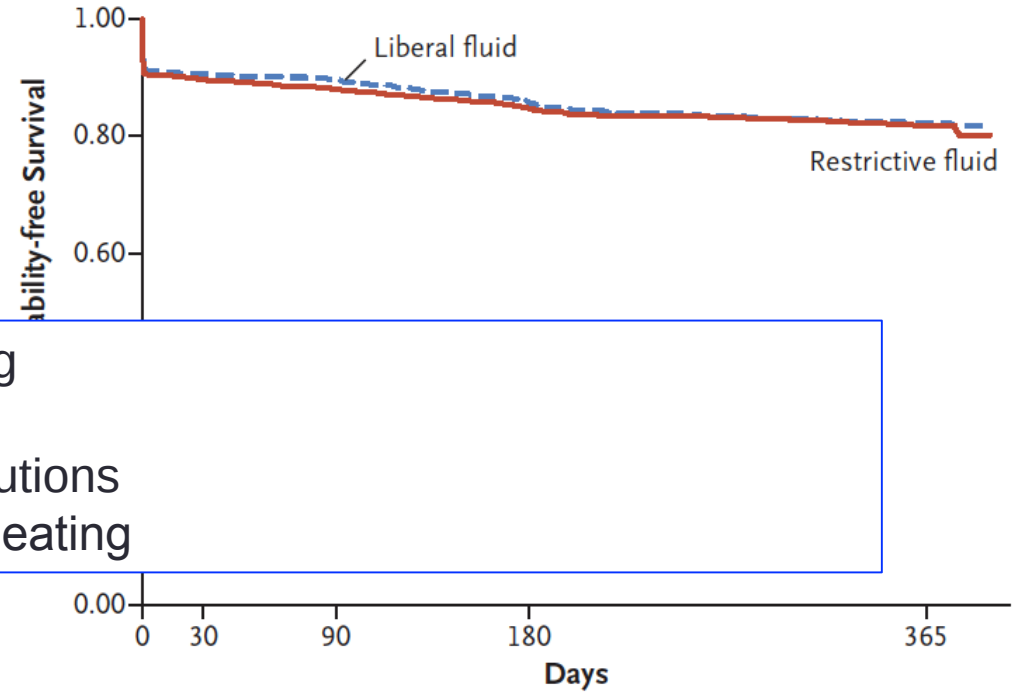
Restrictive versus Liberal Fluid Therapy for Major Abdominal Surgery

P.S. Myles, R. Bellomo, T. Corcoran, A. Forbes, P. Peyton, D. Story, C. Christophi, K. Leslie, S. McGuinness, R. Parke, J. Serpell, M.T.V. Chan, T. Painter, S. McCluskey, G. Minto, and S. Wallace, for the Australian and New Zealand College of Anaesthetists Clinical Trials Network and the Australian and New Zealand Intensive Care Society Clinical Trials Group*

RELIEF Trial: Liberal vs Restrictive Fluid Therapy

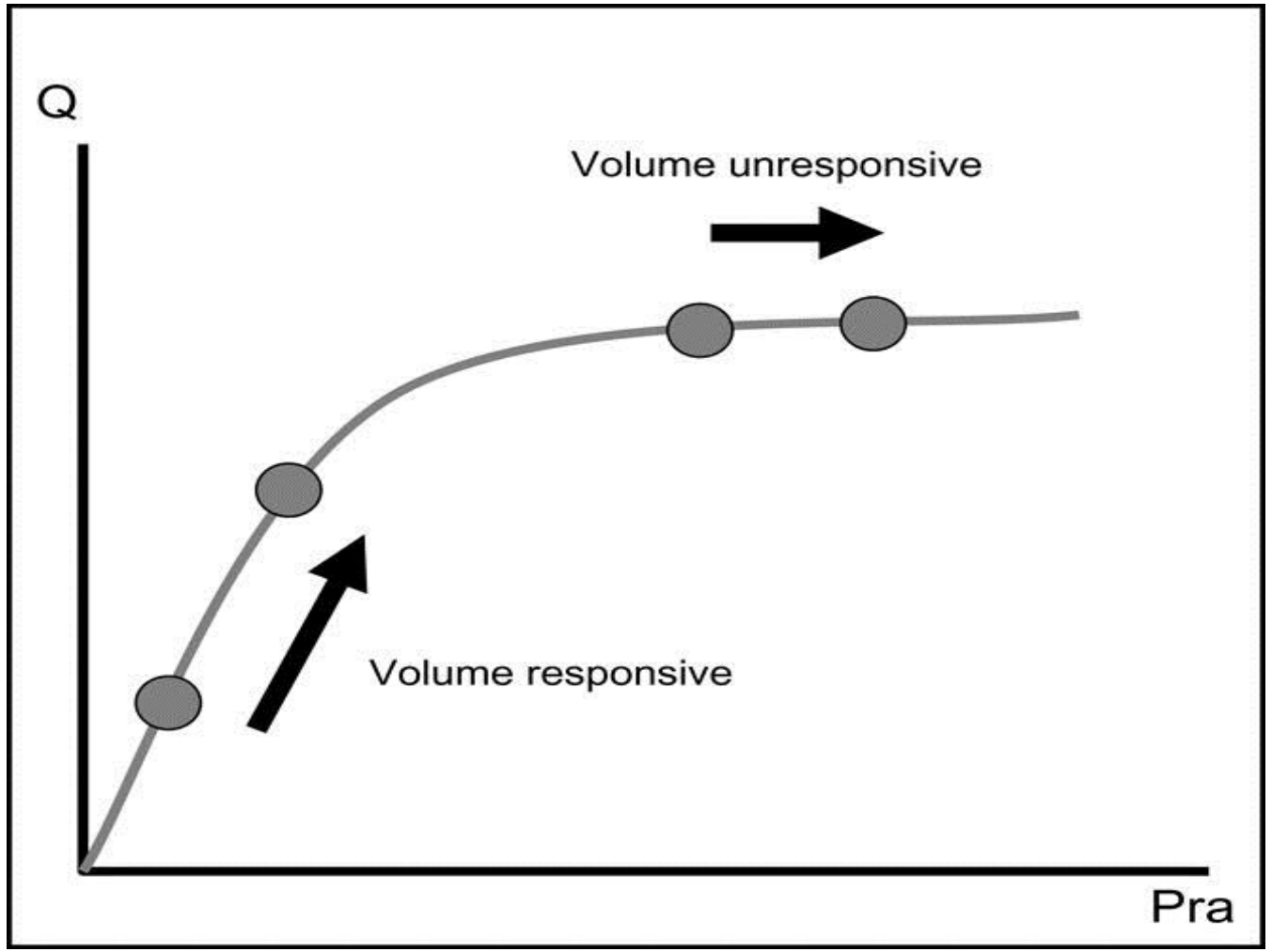
- A pragmatic, trial of 3000 pts major abdominal surgery
- Restrictive or liberal iv fluid regimen during & for up to 24 h after surgery.
- Primary outcome was disability-free survival at 1 year. Secondary outcomes were AKI at 30 days, RRT at 90 days, and a composite of septic complications, surgical-site infection, or death.
- Resu
  - Re
  - Th
  - AK
    (P<0.001).
  - RRT (0.9% vs. 0.3%, P = 0.048) were higher in the restrictive fluid group, bu the between-group difference was not significant after adjustment for multiple testing.
- CONCLUSIONS. A restrictive fluid regimen was not associated with a higher rate of disability-free survival than a liberal fluid regimen and was associated with a higher rate of AKI.

WT: 1.6 kg vs 0.3 kg
Minimally invasive
Hypotonic, balanced solutions
1/3 not eating and ½ not eating



PS Myles et al. N Engl J Med 378;24

Fluid Management in the Critically Ill Patient



Magder S:Curr Opin Crit Care 2005;11:264-270

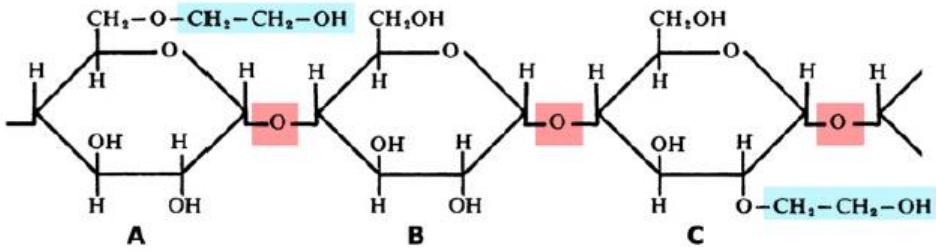
WHAT TYPE OF FLUIDS SHOULD BE ADMINISTERED?

Colloid vs Crystalloid?

Balanced Solutions vs NS?

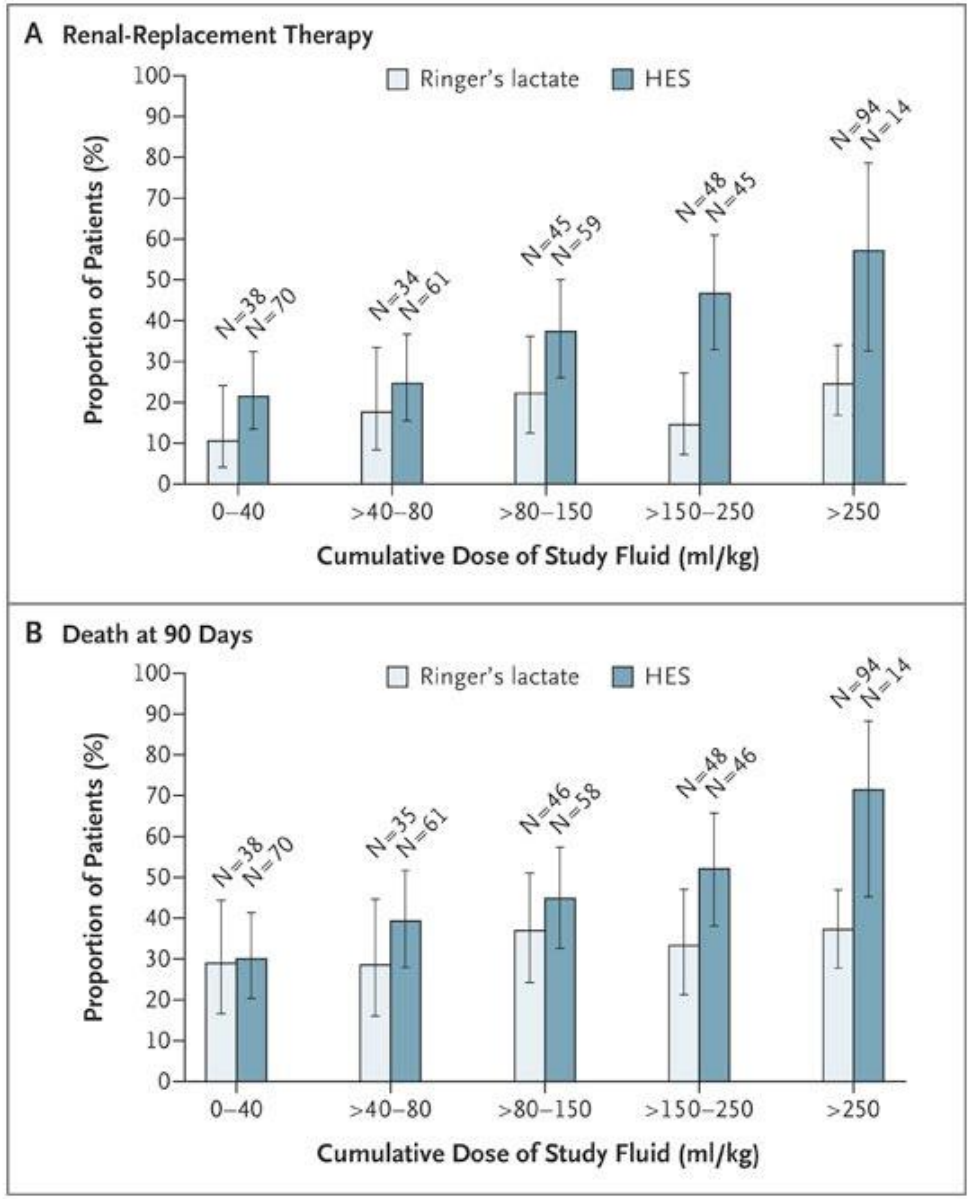
What type of fluids?

- Controversy - colloid vs crystalloid
- 1999, launch of new generation of hydroxyethyl starch (HES), tetrastarch as a promising colloid to restore circulation
- Tens of millions of patients were treated with yearly sales of hundreds of millions of dollars
- Colloid solutions may minimize resuscitation volumes, and may sustain intravascular volume
- Based upon physiological models and small studies
- Crystalloid solutions are inexpensive and readily available
- Recent publications have shed new light on the use of HES



Colloid vs Crystalloid in Sepsis

- Severe septic pts received either 10% pentastarch (HES), or modified Ringer's lactate for fluid resuscitation.
- The rate of death at 28 days did not differ significantly between the HES group and the Ringer's lactate group (26.7% and 24.1%,P=0.48).
- Correlation between the cumulative dose of HES and
  - the need for renal-replacement therapy
  - the rate of death at 90 days
- There was no corresponding correlation with the cumulative dose of Ringer's lactate



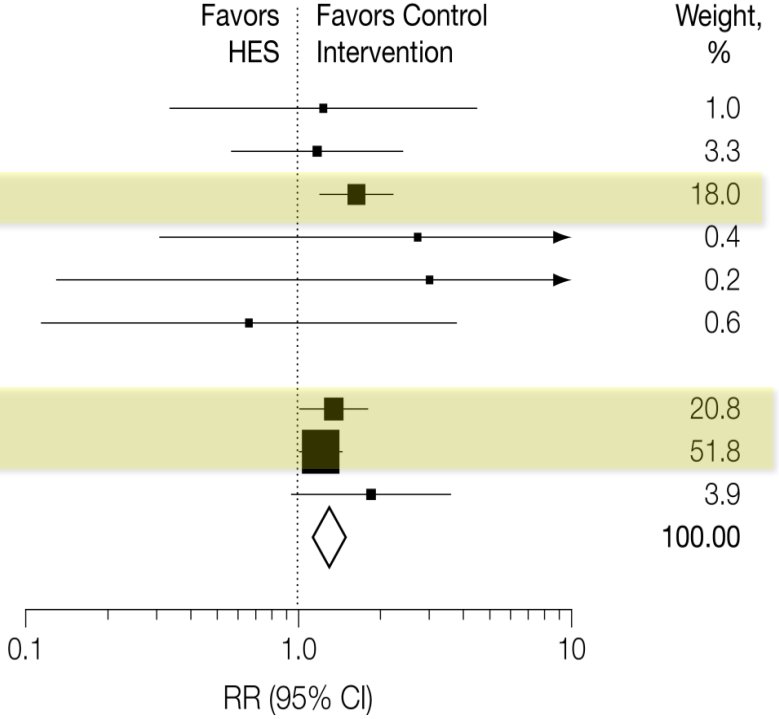
Frank M. Brunkhorst, NEJM: 358:125-139, 2008

Association of Hydroxyethyl Starch Administration With Mortality and Acute Kidney Injury in Critically Ill Patients Requiring Volume Resuscitation: *A Systematic Review and Meta-analysis*

Source	HES No. of Events	HES Total	Control No. of Events	Control Total	RR (95% CI)
Berard et al,[26] 1995	5	155	4	152	1.23 (0.34-4.48)
Schortgen et al,[3] 2001	13	65	11	64	1.16 (0.56-2.40)
Brunkhorst et al,[44] 2008 VISEP	81	297	51	303	1.62 (1.19-2.21)
McIntyre et al,[22] 2008	3	21	1	19	2.71 (0.31-23.93)
Du et al,[35] 2011	1	21	0	21	3.00 (0.13-69.70)
James et al,[4] 2011	2	58	3	57	0.66 (0.11-3.78)
Viachou et al,[37] 2010	0	12	0	17	Not estimable
Perner al,[53] 2012 6S	87	400	65	400	1.34 (1.00-1.79)
Myburgh et al,[54] 2012 CHEST	235	3500	196	3500	1.20 (1.00-1.44)
Guidet et al,[52] 2012	21	100	11	96	1.83 (0.93-3.59)
Total (95% CI)		**4629**		**4629**	**1.32 (1.15-1.50)**
Total events	448		342		

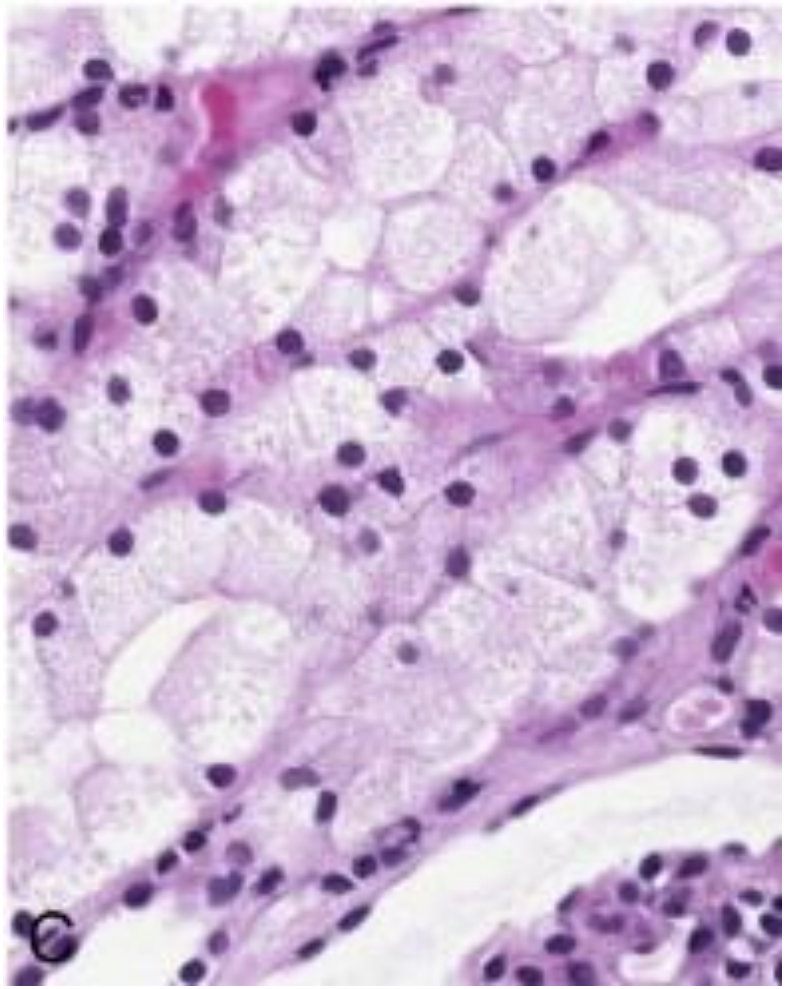
Heterogeneity: $\tau^2 = 0.00$; $\chi^2_8 = 5.07$; ($P = .75$); $I^2 = 0\%$

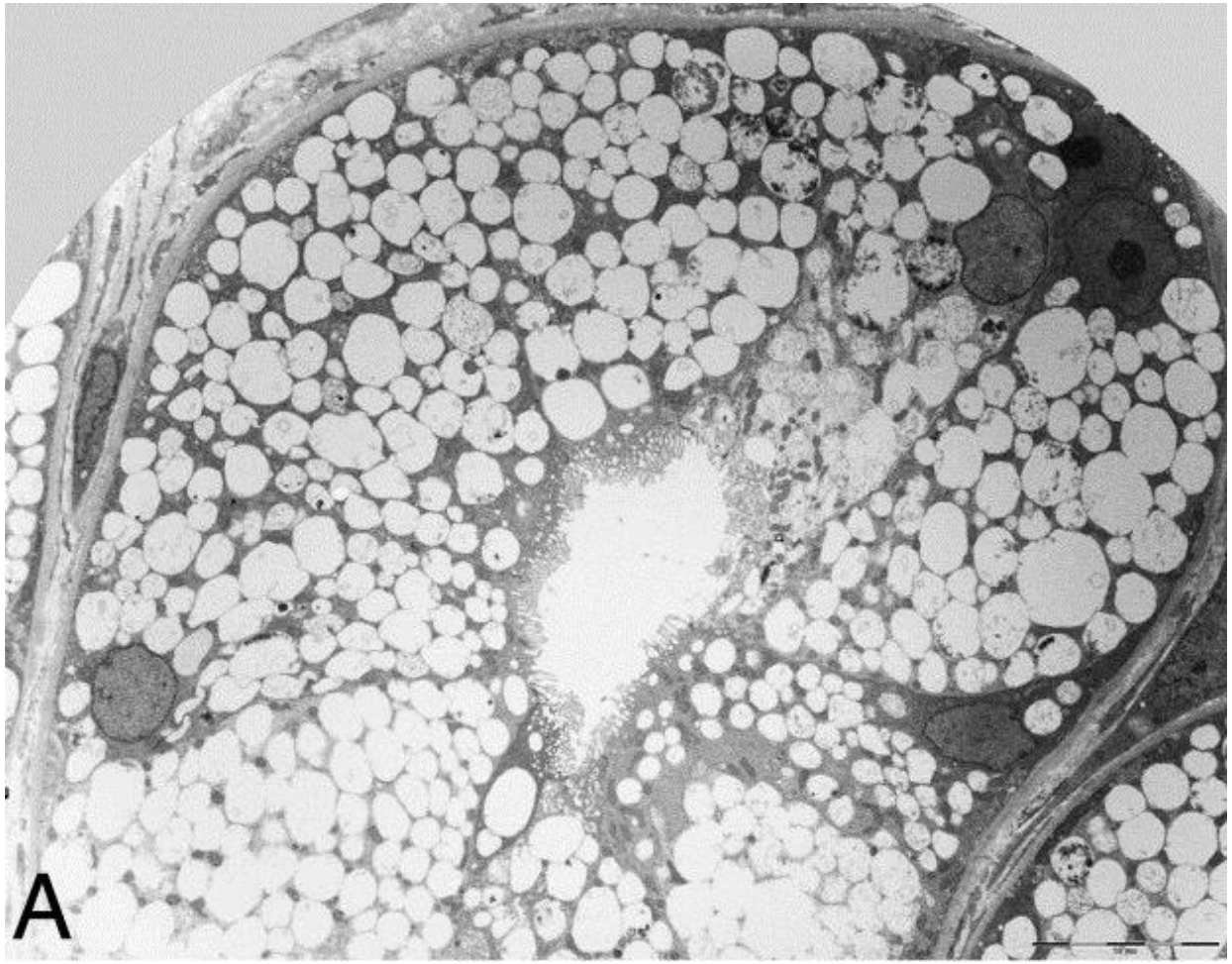
Test for overall effect: $Z = 4.08$, ($P < .001$)



JAMA. 2013;309(7):678-688.

Osmotic Nephrosis from Starches





M Dickenmann et al AJKD 51:491-503, 2008

CJ Widermann and M. Joannidis Intens Care Med 40:160-170, 2014

A comparison of albumin and saline for fluid resuscitation in the intensive care unit: SAFE Study

- Multicenter, randomized, double-blind trial to compare the effect of fluid resuscitation with albumin or saline on mortality in the ICU.
- Random assignment - 3497 were assigned to receive albumin and 3500 to receive saline - 4 percent albumin or normal saline for iv-fluid resuscitation during the next 28 days. The two groups had similar baseline characteristics.
- No significant difference in deaths, proportion of with new single or multiorgan failure, # days in ICU, LOS, mechanical ventilation, or days of RRT,
- Conclusion: In patients in the ICU, use of either 4 percent albumin or normal saline for fluid resuscitation results in similar outcomes at 28 days.

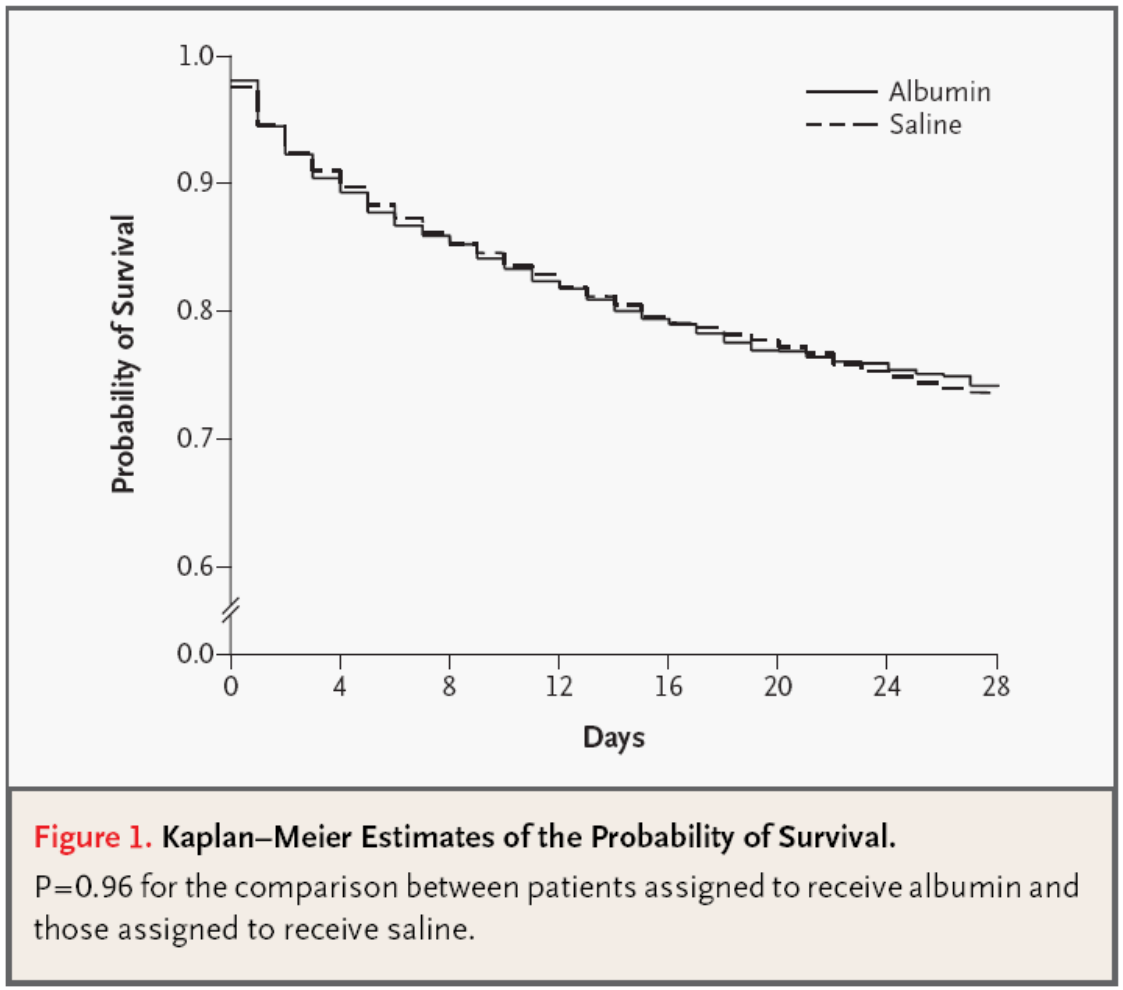


Figure 1. Kaplan–Meier Estimates of the Probability of Survival.
P=0.96 for the comparison between patients assigned to receive albumin and those assigned to receive saline.

S. Finfer et al. NEJM 2004 350;22:2247-56.

Albumin Function: More than oncotic pressure

- Oncotic pressure
- Ligand binding-transport of various molecules
  - Bilirubin, metals, thyroxine, tryptophan
  - Drugs: warfarin, diazepam, ibuprofen
  - Transports NO as S-nitroso-albumin
- Antioxidant and anti-inflammatory
  - Free radical scavenging
  - Modulate capillary permeability, neutrophil adhesion and activation and its hemostatic effects.
- Endothelial stabilization

Wong, F. Nature 2007. Clin Pract Gastro and Hepatol 4: 43-50.
Halliwell, B. 1988, Biochem Pharmacol 37:569-571
Evans, TW. 2002 Aliment Pharmacol Ther 16: (suppl 5) 6-11.

Summary for use of HES vs Crystalloid Solutions

"There is no evidence from randomized controlled trials that resuscitation with colloids reduces the risk of death, compared to resuscitation with crystalloids, in patients with trauma, burns or following surgery. Furthermore, the use of hydroxyethyl starch might increase mortality. As colloids are not associated with an improvement in survival and are considerably more expensive than crystalloids, it is hard to see how their continued use in clinical practice can be justified."

Perel P, Roberts I, Ker K. Cochrane Database Syst Rev. 2013 Feb 28;2:CD000567

AKI in ICU: Cl-liberal vs Cl restrictive

Cl restrictive strategy associated with decrease incidence of AKI

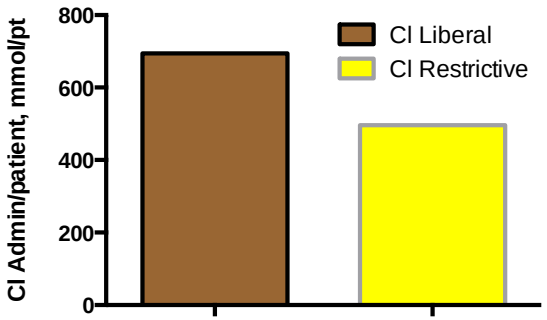
- Prospective, open-label, sequential period pilot study
- 760 patients admitted to ICU during the control period (6 mo) vs 773 patients admitted during the intervention period
- **Cl Liberal Period:** standard IV fluids then 6-month phase-out period followed by
- **Cl Restrictive Period:** use of chloride-rich was restricted
- **Results**
  - Chloride administration decreased from 694 to 496 mmol/patient) from the control period to the intervention period.
  - Serum creatinine level increase while in the ICU was .26 mEQ/L vs 0.17 mEQ/L (P=0.03)
  - There were no differences in hospital mortality, hospital or ICU length of stay, or need for RRT after hospital discharge.
- **Conclusion:** Chloride-restrictive strategy was associated with a significant decrease in the incidence of AKI and use of RRT.

Table 2. Composition of Trial Fluids[a]

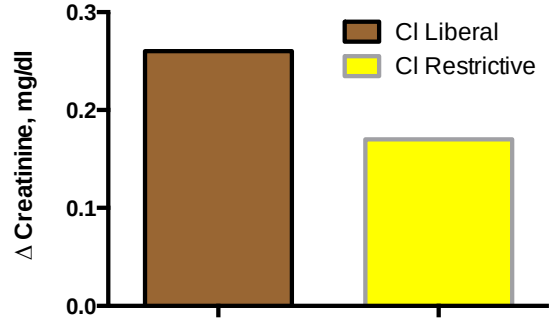
	0.9% Saline	Hartmann	4% Gelatin	Plasma-Lyte 148	Albumin 4%	Albumin 20%
Sodium	150	129	154	140	140	48-100
Potassium	0	5	0	5	0	0
Chloride	150	109	120	98	128	19
Calcium	0	2	0	0	0	0
Magnesium	0	0	0	1.5	0	0
Lactate	0	29	0	0	0	0
Acetate	0	0	0	27	0	0
Gluconate	0	0	0	23	0	0
Octanoate	0	0	0	0	6.4	32

[a] All concentrations in mmol/L.

Cl Administration



AKI



N.M. Yunos et al. JAMA. 2012;308(15):1566-1572

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Balanced Crystalloids versus Saline in Critically Ill Adults

Matthew W. Semler, M.D., Wesley H. Self, M.D., M.P.H., Jonathan P. Wanderer, M.D., Jesse M. Ehrenfeld, M.D., M.P.H., Li Wang, M.S., Daniel W. Byrne, M.S., Joanna L. Stollings, Pharm.D., Avinash B. Kumar, M.D., Christopher G. Hughes, M.D., Antonio Hernandez, M.D., Oscar D. Guillamondegui, M.D., M.P.H., Addison K. May, M.D., Liza Weavind, M.B., B.Ch., Jonathan D. Casey, M.D., Edward D. Siew, M.D., Andrew D. Shaw, M.B., Gordon R. Bernard, M.D., and Todd W. Rice, M.D., for the SMART Investigators and the Pragmatic Critical Care Research Group*

The NEW ENGLAND JOURNAL of MEDICINE

Balanced crystalloids – lower rate of the composite outcome of death from any cause, new renal-replacement therapy, or persistent renal dysfunction than the use of saline.

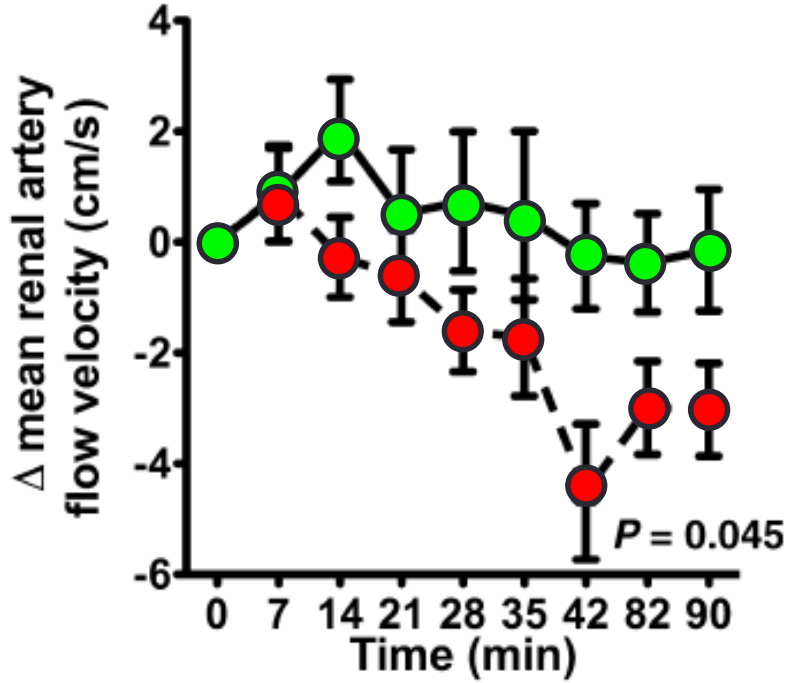
ORIGINAL ARTICLE

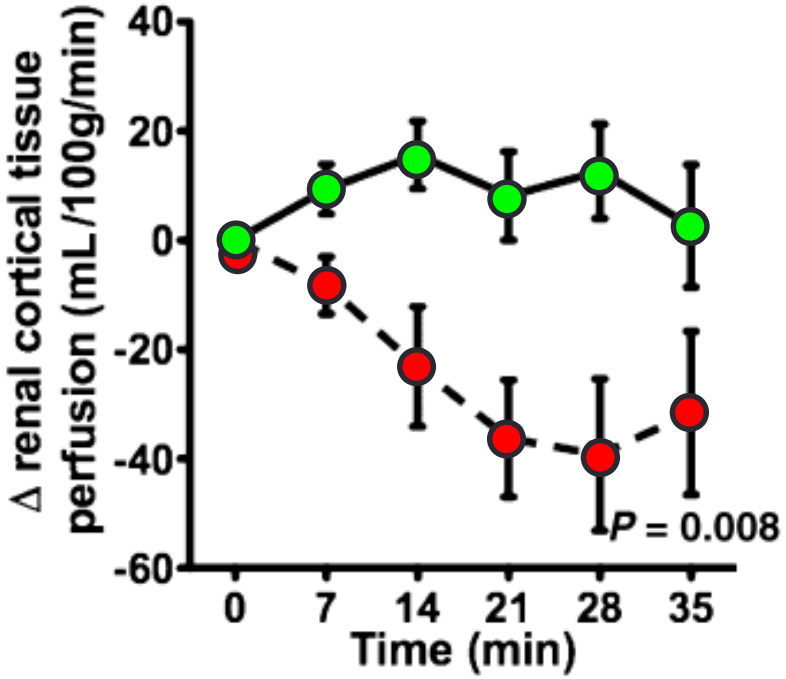
Balanced Crystalloids versus Saline in Noncritically Ill Adults

Wesley H. Self, M.D., M.P.H., Matthew W. Semler, M.D., Jonathan P. Wanderer, M.D., Li Wang, M.S., Daniel W. Byrne, M.S., Sean P. Collins, M.D., Corey M. Slovis, M.D., Christopher J. Lindsell, Ph.D., Jesse M. Ehrenfeld, M.D., M.P.H., Edward D. Siew, M.D., Andrew D. Shaw, M.B., Gordon R. Bernard, M.D., and Todd W. Rice, M.D., for the SALT-ED Investigators*

There was no difference in hospital-free days between treatment with balanced crystalloids and treatment with saline. Balanced crystalloids resulted in a lower incidence of major adverse kidney events within 30 days than saline (P=0.01).

Intravenous infusion of infusion of 0.9% saline results in reductions in renal blood cortical perfusion





Plasma-Lyte 148

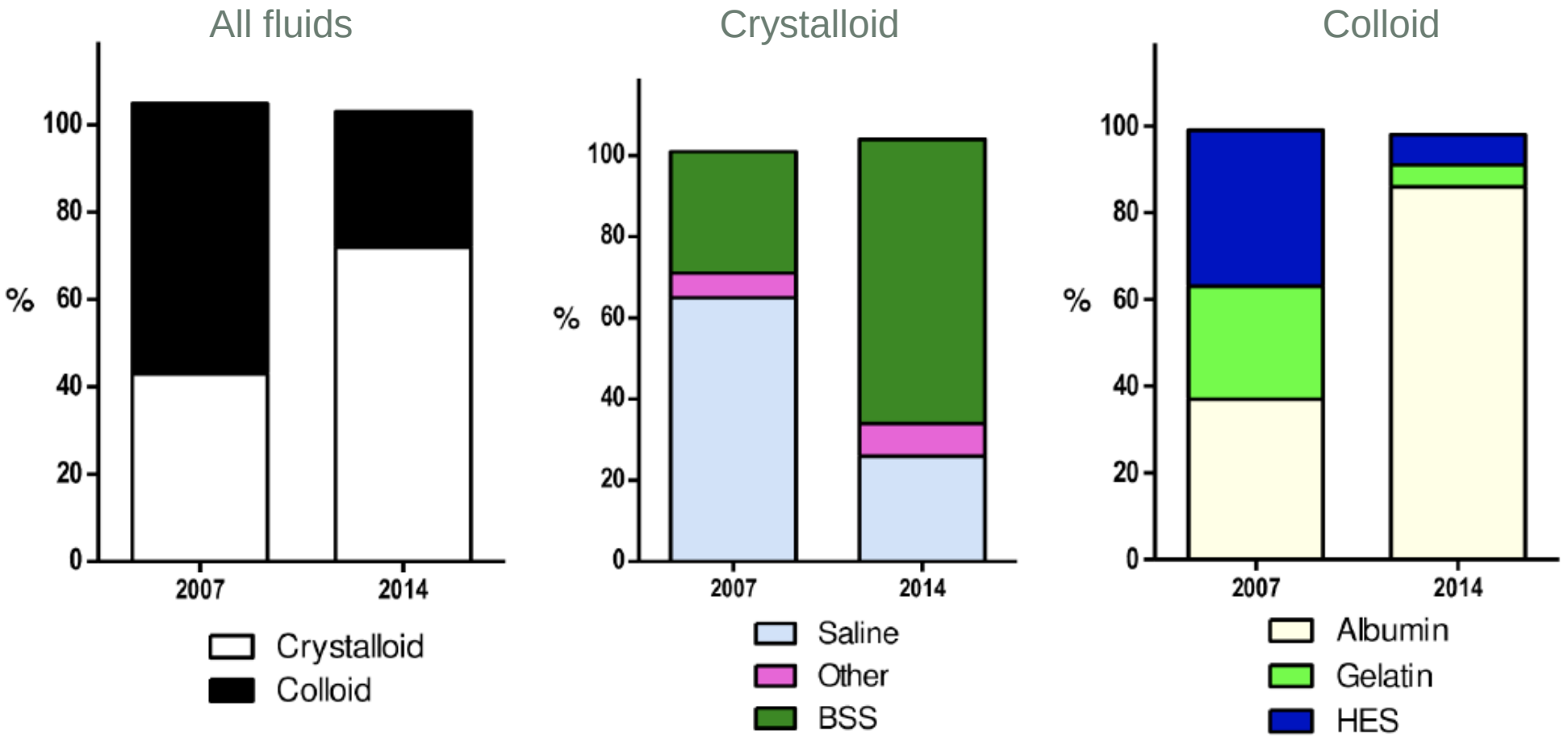
0.9% Saline

2 L over 1 hr

Phase Contrast Angiography MRI

AH Chowdhury… DN Lobo Ann Surg 256: 18-24, 2012

Proportion of all fluid resuscitation episodes given in 2007 and 2014 in 84 ICUs



NE Hammond et al. PLoS One 12: e0176292, 2017

AKI and Fluid Management

- Fluid overload leads to a delayed recognition and underestimation of severity.
- Prolonged fluid resuscitation leads to edema in the kidneys and other organs
- Fluid overload is associated with increased morbidity and mortality.
- An early transition to a fluid-restrictive strategy might be beneficial in patients with AKI
- The type of fluid used in resuscitation is important
  - Starches have been shown to to aggravate kidney function leading to AKI
  - Cl restrictive fluid strategy may have advantages (followup studies)
- Prevention of fluid overload may be an important and under-appreciated determinant of survival and is evolving as a primary trigger for initiation of RRT
- CRRT>IHD in fluid removal
  - Improved renal recovery?

Modified from Prowle et al. Nature Reviews Nephrol 2010;6:107-115

ACUTE KIDNEY INJURY AND FLUID MANAGEMENT

Questions??

mdo7@virginia.edu