Fluid Management in Critically Ill AKI Patients

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KO/MG31/15-0017

Outline

- ***Fluid balance in critically ill patients:***
  General considerations
- Fluid balance in critically ill AKI patients and RRT
- Which modality is better : IHD vs CRRT
- When to initiate RRT

AKI in critically ill patients

- incidence of AKI in ICU : 20-35%
- incidence of RRT requiring AKI in ICU : 5-6%
- high mortality (~50%)
- Fluid therapy : key intervention in management of critical illness

Rivers et.al. NEJM, 2001

Acute Kidney Injury (AKI)

-reduced cardiac output

-systemic hypotension

-triggered neuroendocrine reflexes

Vigorous iv fluid administration

-expand intravascular vol

-maintain cardiac output

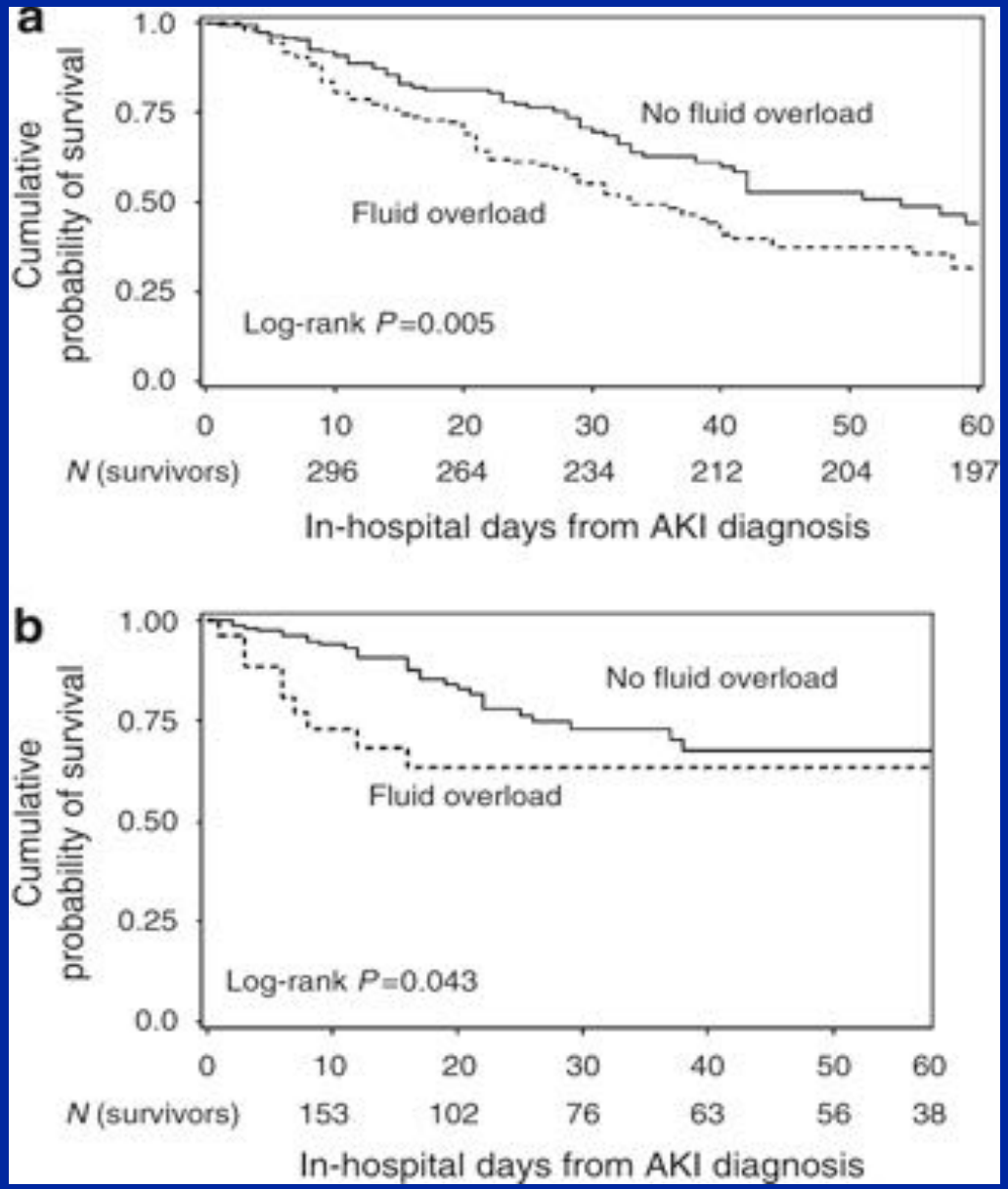
& organ perfusion

Positive fluid balance :

-worsening organ dysfunction

-worse postoperative outcome

Fluid status and mortality in AKI patients-PICARD



dialysis

no dialysis

Bouchard et.al. Kidney Int, 2009

Fluid status and mortality in AKI

Mortality (60 day) Hazard Ratios

-Sepsis Occurrence in Acutely Ill Patients (SOAP) study-

Hazard ratios: results of multivariate Cox regression analysis for 60-day mortality in critically ill patients with 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 hours	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

1L of positive fluid balance during 24 hr : 20% increase in mortality risk

Payen et.al. Crit Care, 2008

Fluid management-Acute Lung Injury (ALI)

Table 3. Main Outcome Variables.*

-136ml/wk +6992/wk

Outcome	Conservative Strategy	Liberal Strategy	P Value
Death at 60 days (%)	25.5	28.4	0.30
Ventilator-free days from day 1 to day 28†	14.6±0.5	12.1±0.5	<0.001
ICU-free days†			
Days 1 to 7	0.9±0.1	0.6±0.1	<0.001
Days 1 to 28	13.4±0.4	11.2±0.4	<0.001
Organ-failure–free days†‡			
Days 1 to 7			
Cardiovascular failure	3.9±0.1	4.2±0.1	0.04
CNS failure	3.4±0.2	2.9±0.2	0.02
Renal failure	5.5±0.1	5.6±0.1	0.45
Hepatic failure	5.7±0.1	5.5±0.1	0.12
Coagulation abnormalities	5.6±0.1	5.4±0.1	0.23
Days 1 to 28			
Cardiovascular failure	19.0±0.5	19.1±0.4	0.85
CNS failure	18.8±0.5	17.2±0.5	0.03
Renal failure	21.5±0.5	21.2±0.5	0.59
Hepatic failure	22.0±0.4	21.2±0.5	0.18
Coagulation abnormalities	22.0±0.4	21.5±0.4	0.37
Dialysis to day 60			
Patients (%)	10	14	0.05
Days	11.0±1.7	10.9±1.4	0.96

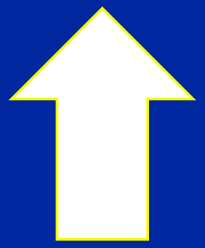
The National Heart, Lung, and Blood Institute Acute Respiratory Distress Syndrome (ARDS) Clinical Trials Network. N Engl J Med , 2006

Potential adverse effects of fluid overload

Exogenous fluids

-expand effective circulating volume

-increase cardiac output



extent, duration of volume resuscitation: variable

Preexisting chronic disease

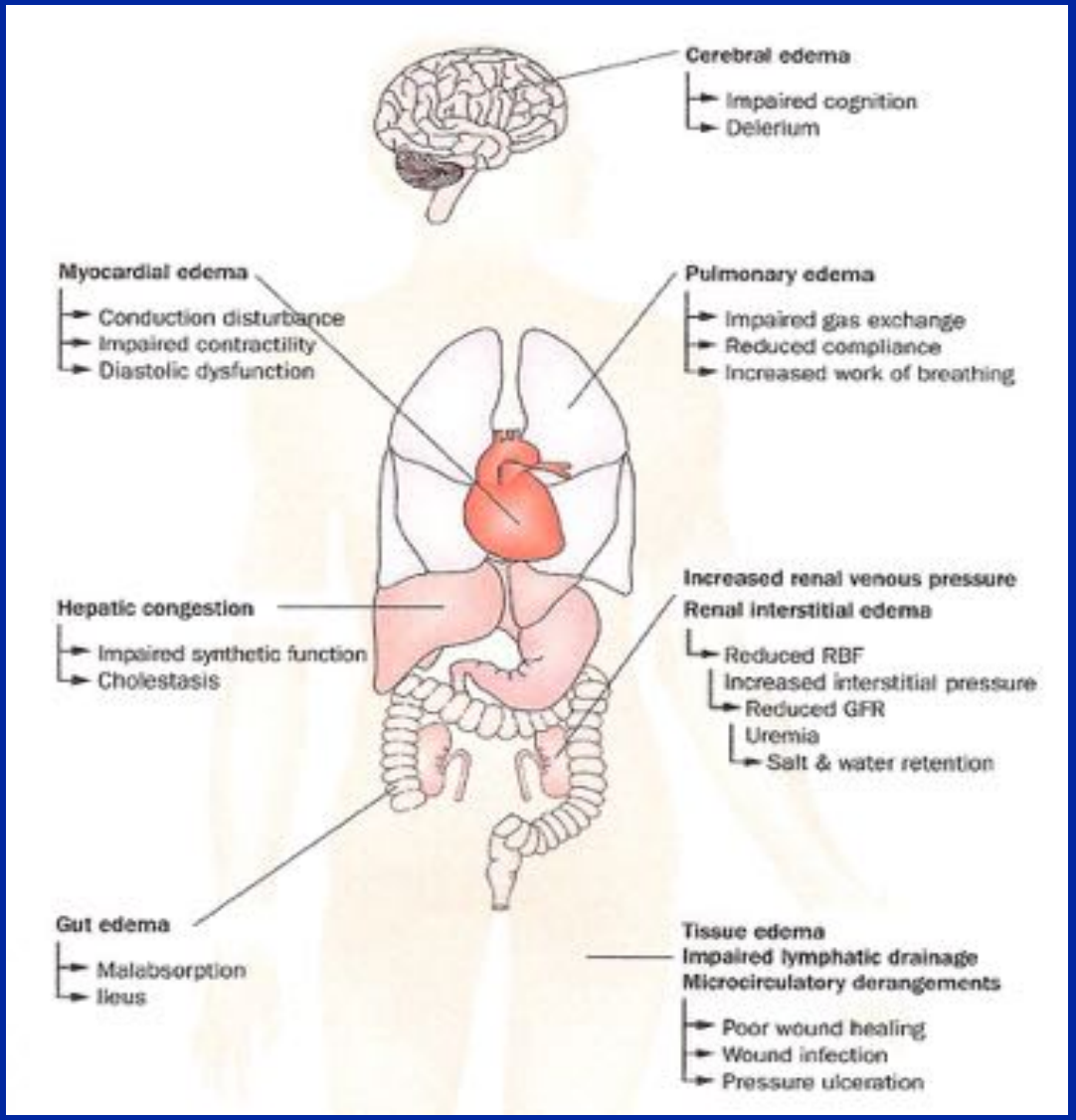
Effects of acute illness

myocardial compliance, contractility, capillary permeability…

impaired Na excretion

Potential Clinical Consequences of Organ Edema in Critically Ill Patients

Prowle et al, Nature Revs Nephrol 2009



- Fluid balance in critically ill patients:

  General considerations

- ***Fluid balance in critically ill AKI patients and RRT***
- Which modality is better : IHD vs CRRT
- When to initiate RRT

Extracorporeal renal replacement therapy (RRT)

- Supportive treatment of AKI
- Decisions to start RRT

  ; volume overload

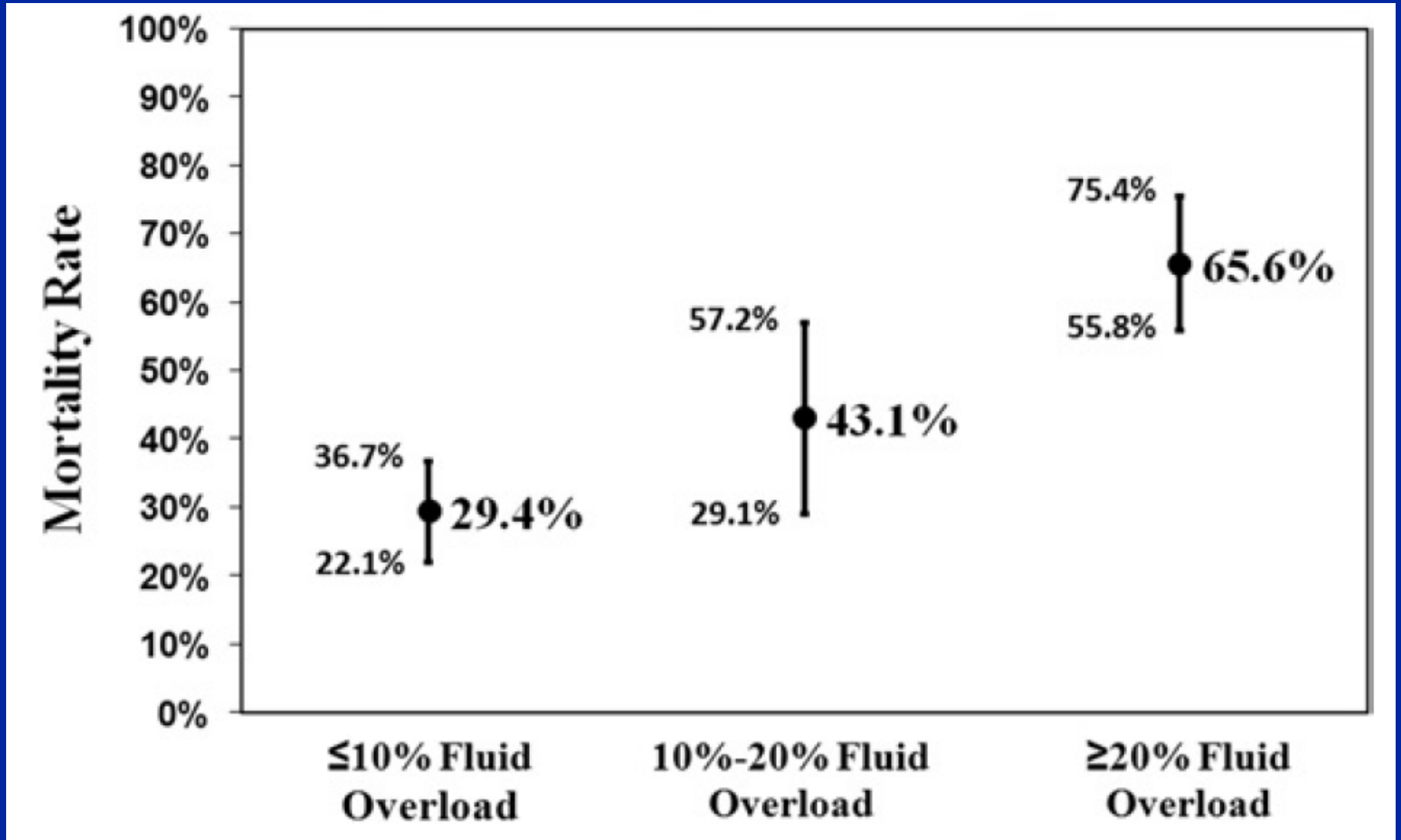
  biochemical abnormalities (azotemia, hyperkalemia,

  severe acidosis..)

$$\text{Percent Fluid Overload (\%FO)} = \frac{\text{total fluid input} - \text{total fluid output}}{\text{baseline body weight}}$$

Fluid Overload in ppCRRT Registry

Sutherland et al, AJKD 2010



Fluid Overload/Mortality Association in FINNAKI

Vaara et al, Crit Care 2014

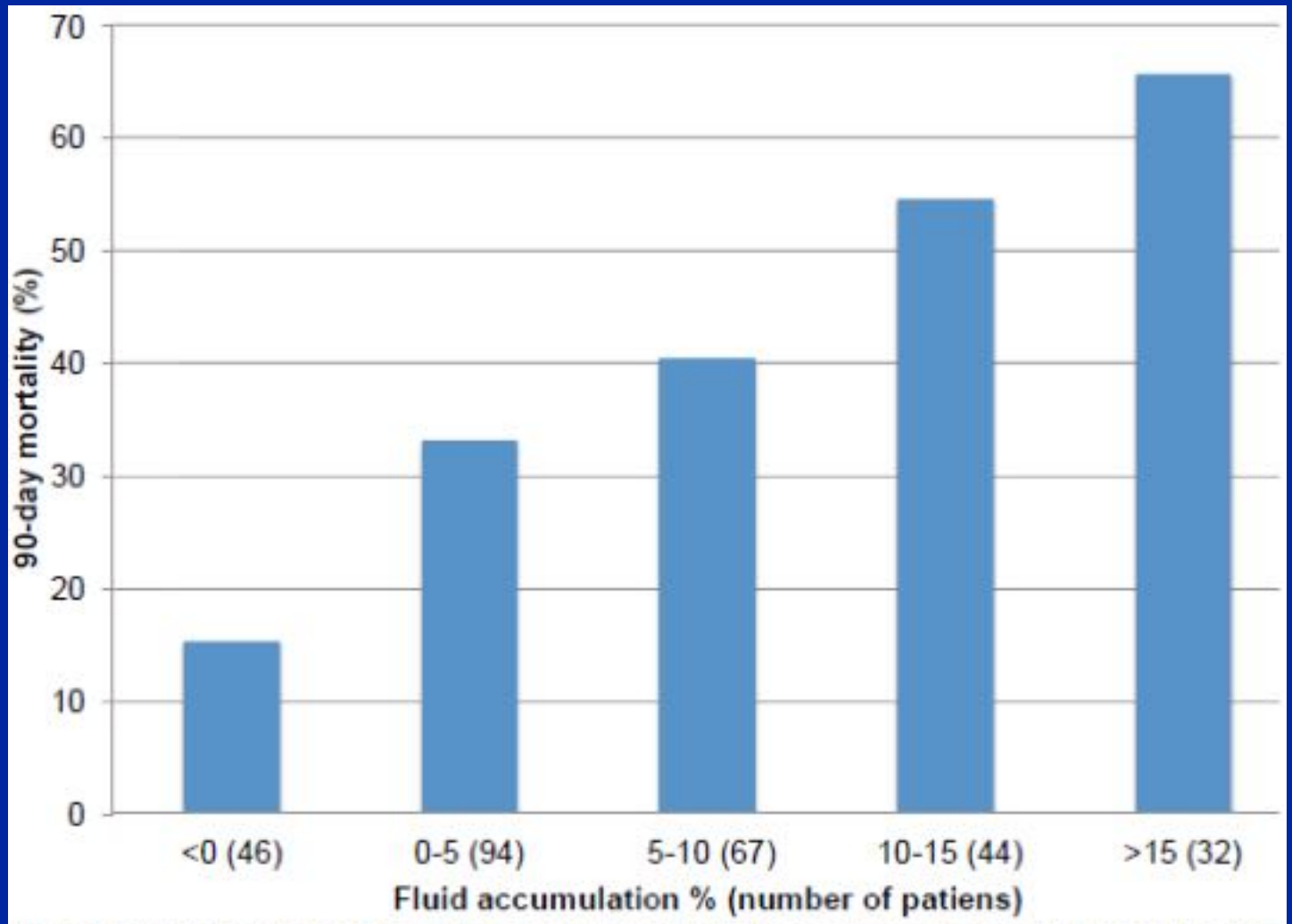


Figure 3 Ninety-day mortality according to the percentage of fluid accumulation prior to renal replacement therapy initiation. *Comparison across groups $P < 0.001$.

Association Between Fluid Balance and Mortality

RENAL Investigators, Crit Care Med 2012

Mean daily fluid balance in survivors : - 234ml/day
Mean daily fluid balance in nonsurvivors : +560ml/day

Variable	Effect (Discrete Variable)	Odds Ratio	95% Confidence Interval	*p*
Negative mean daily fluid balance during index admission to intensive care unit[b]	No vs. yes	0.318	0.24-0.43	<.0001
Age		1.033	1.02-1.04	<.0001
Time from intensive care unit admission to randomization (d)		1.002	1.00-1.04	0.0065
Acute Physiology and Chronic Health Evaluation III score		1.012	1.01-1.02	0.0002
Sequential Organ Failure Assessment liver (score)		1.224	1.07-1.40	0.0033
International normalized ratio for prothrombin time		1.277	1.08-1.51	0.0047

Critical decisions have to be made

-which modality is better for critically ill AKI patients with fluid overload

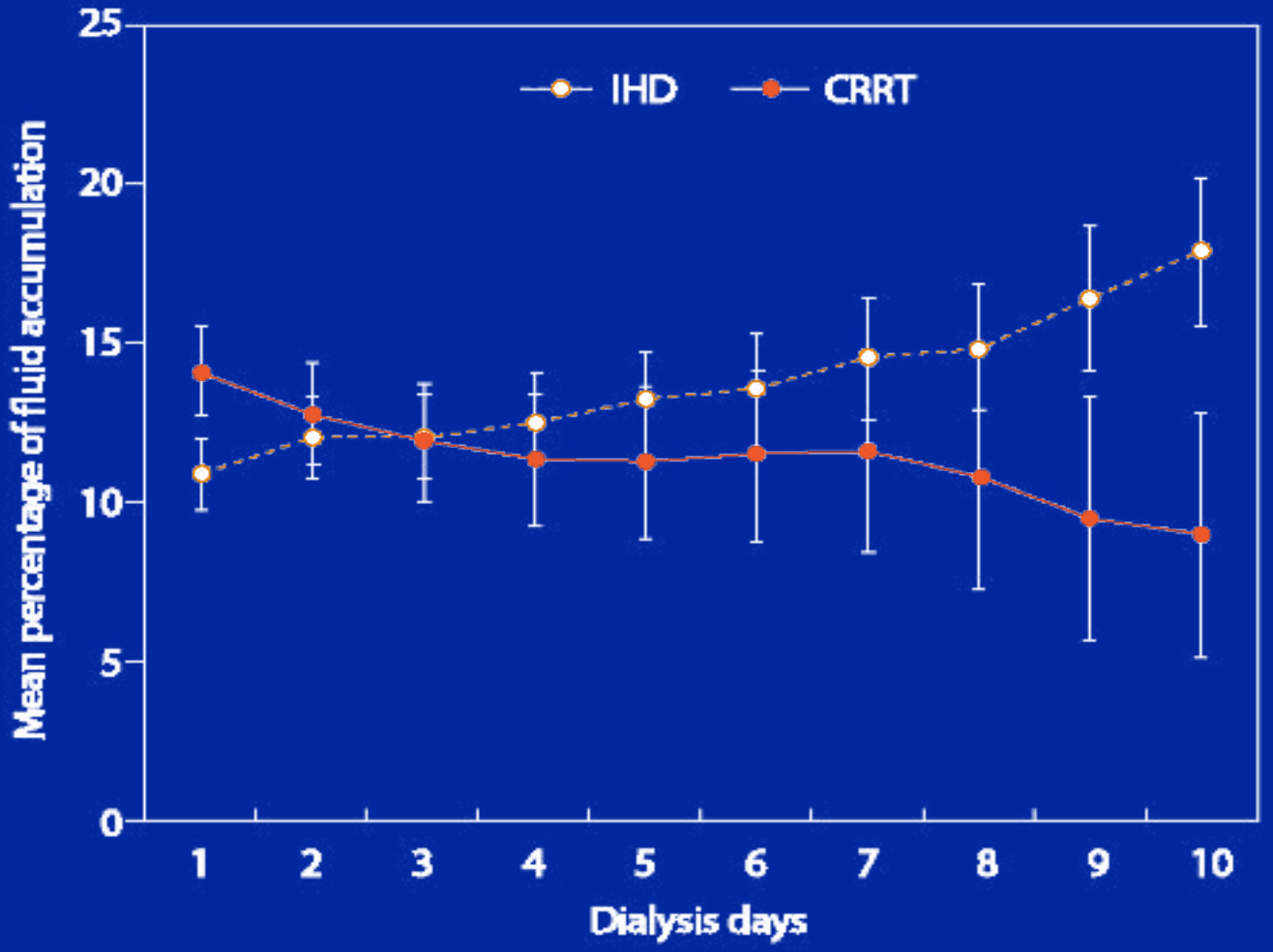
-when to initiate RRT (early vs late)

Modality

(IHD vs CRRT)

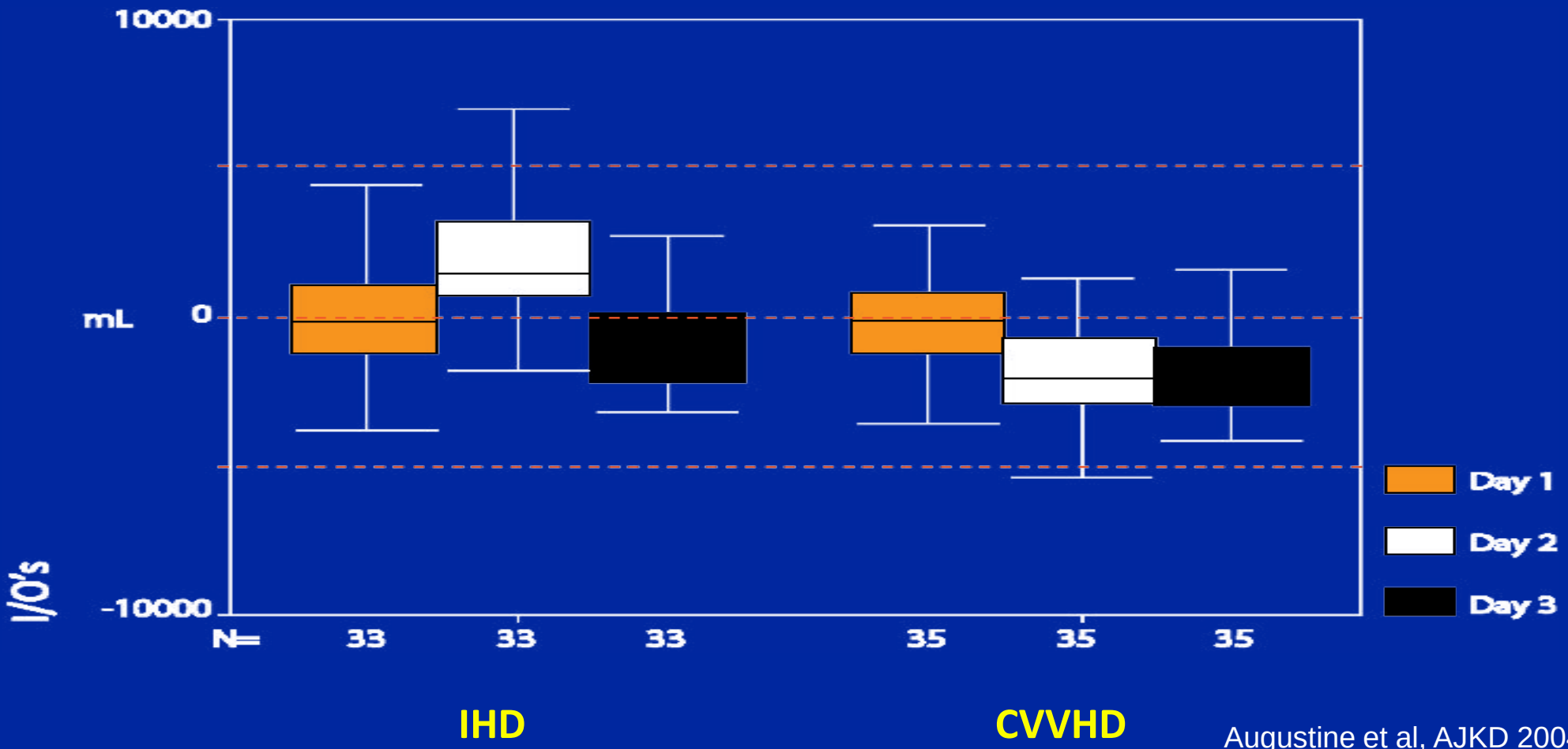
Correction of Fluid Overload: CRRT vs IHD

PICARD study



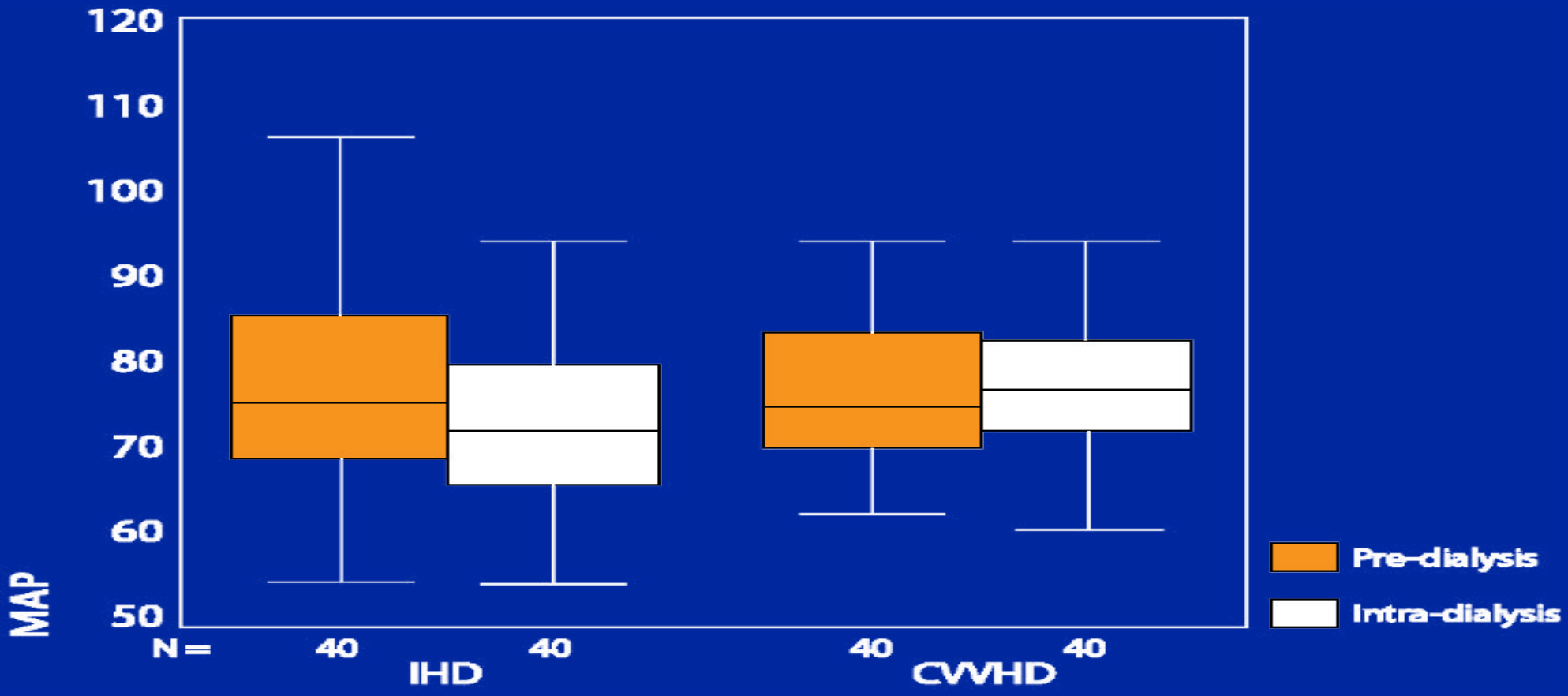
Bouchard et.al. Kidney Int, 2009

Fluid Balance: CRRT vs IHD (RCT, Cleveland clinic)



Augustine et al, AJKD 2004

Hemodynamic Stability: CRRT vs IHD
(RCT, Cleveland clinic)



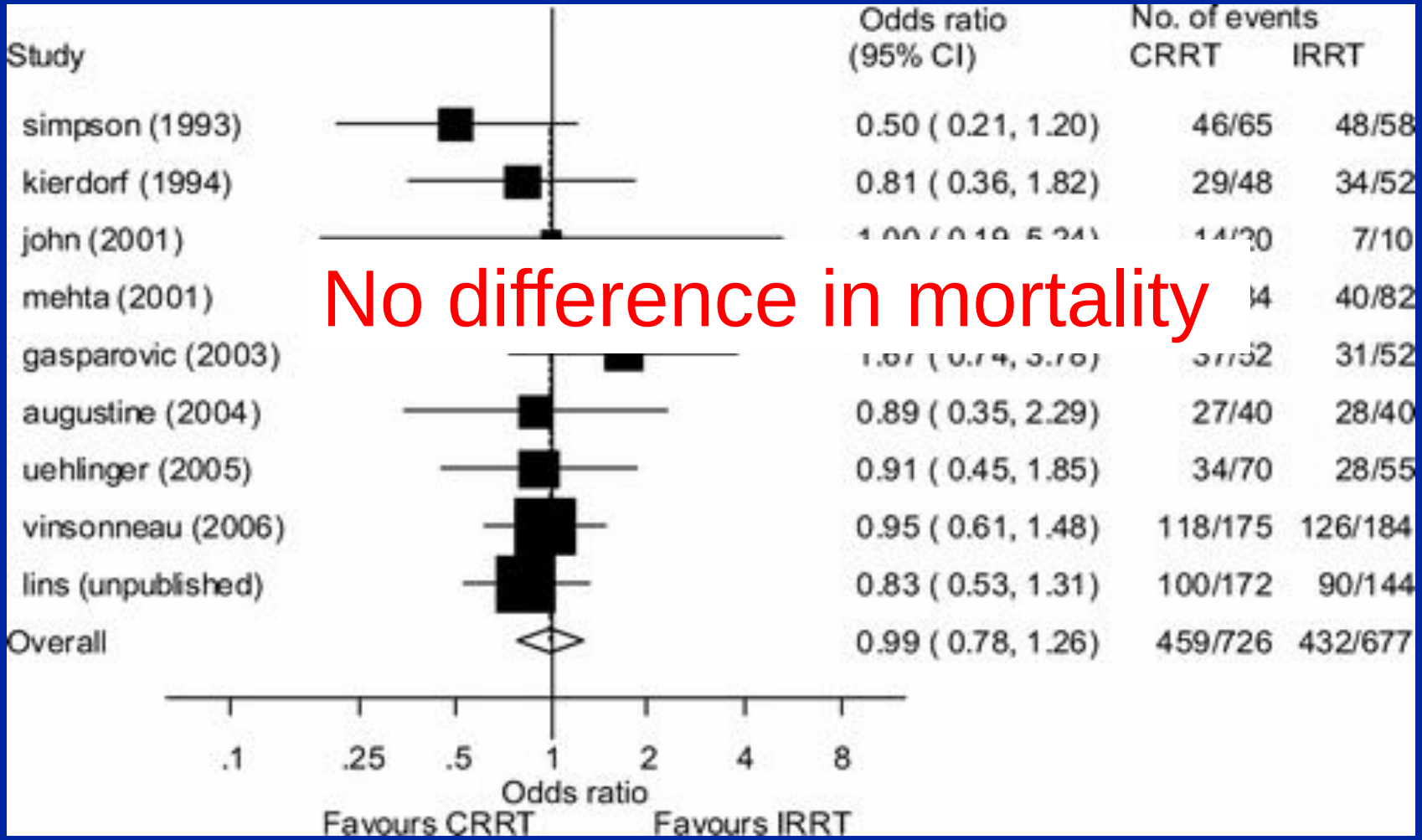
Augustine et al, AJKD 2004

Outcome (IRRT vs CRRT)

	IRRT	CRRT	*P*-value
Number of AKI patients	*n* = 144	*n* = 172	
Hospital mortality	62.5%	58.1%	0.430
ICU and hospital stay			
Days in ICU: mean (SD)	17.2 (18.7)	18.7 (19.0)	0.510
Days in hospital: mean (SD)	31.4 (29.7)	36.8 (31.0)	0.345
Renal outcome in survivors			
CKD stage 1–2 (GFR ≥60 ml/min)	29.8%	28.8%	
CKD stage 3 (GFR 30–59 ml/min)	29.8%	28.8%	
CKD stage 4 (GFR 15–29 ml/min)	14.9%	25.5%	
CKD stage 5 (GFR <15 ml/min or ESKD)	25.5%	16.9%	0.474

Lins et.al. NDT, 2009

Outcome (IRRT vs CRRT) : meta analysis



Bagshaw et.al. Crit Care Med, 2008

When to initiate RRT

(early vs late)

- Optimal timing of RRT : ??

- Classical indications of RRT

  -refractory acidemia

  -refractory hyperkalemia

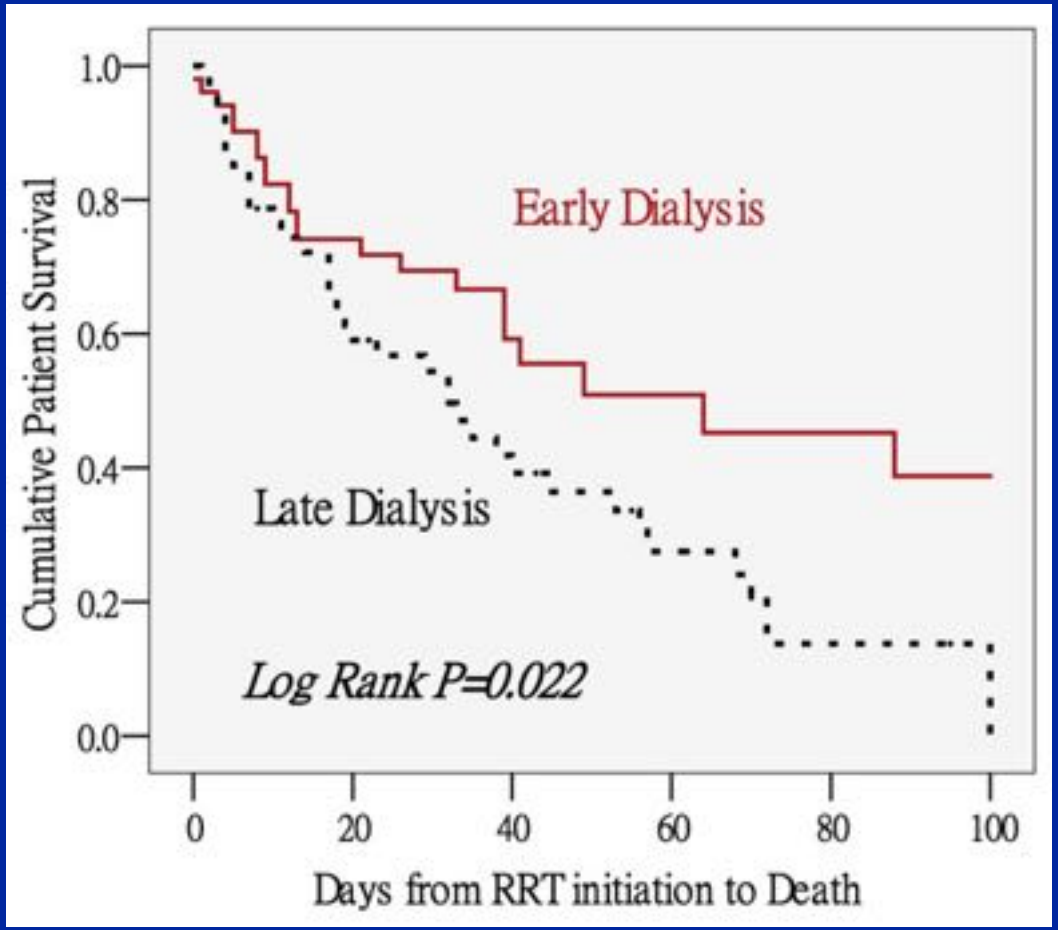
  -fluid overload contributing to pulmonary edema

- Several observational studies: benefit of early RRT
- Early RRT : better control of FO, uremic control

  vs harms of RRT (ex: hypotension..)

Timing of CRRT in septic AKI (I)

multicenter, prospective, observational study
-98 patients with abdominal surgery with postop AKI
-in hospital mortality : 58.2%



Shiao et.al. Crit Care, 2009

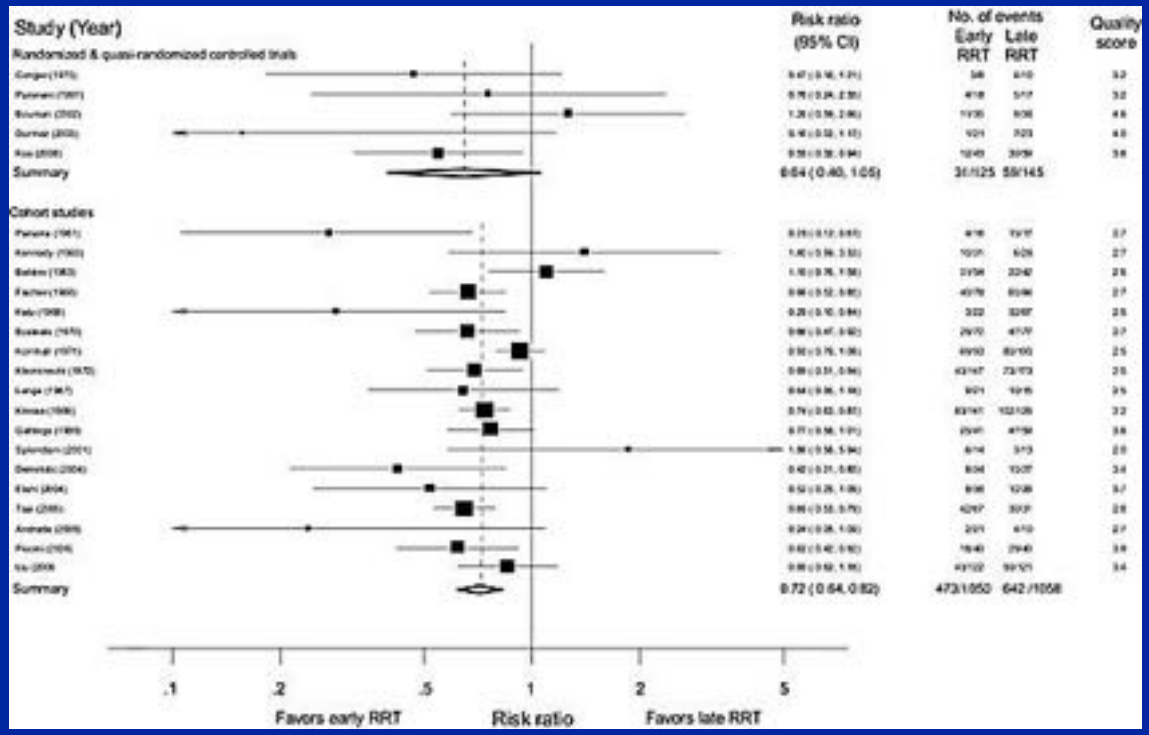
Timing of CRRT in septic AKI : meta analysis

Meta-analysis (Seabra et.al. AJKD, 2008)

23 studies (5 RCT, 1 prospective, 16 retrospective cohort studies)

; -nonsignificant 36% mortality risk reduction (RCT)

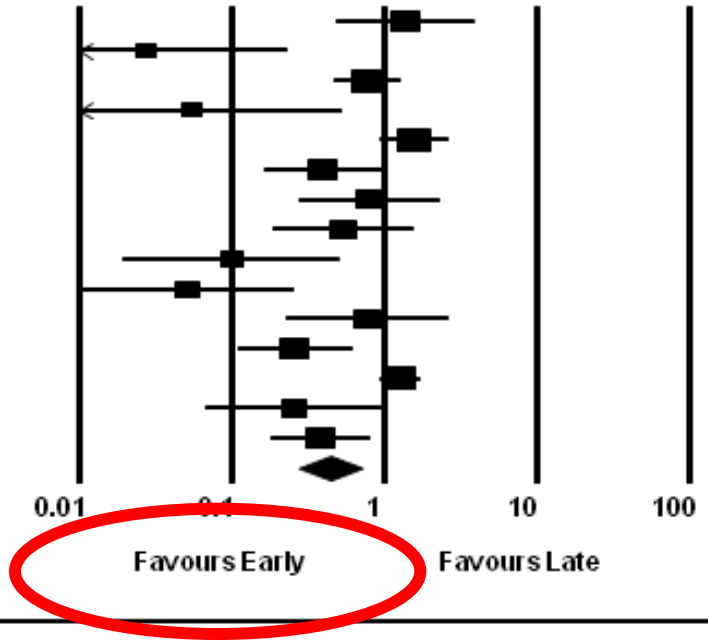
-statistically significant 28% mortality risk reduction (Cohort)



Early vs Late : meta analysis

Meta Analysis: All 15 studies

Study name	Subgroup within study	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Bouman 2002	Mixed	1.375	0.487	3.884	0.601	0.548
Sugahara 2004	Surgery	0.028	0.003	0.231	-3.318	0.001
Liu 2006	Mixed	0.773	0.460	1.298	-0.974	0.330
Sabater 2008	Mixed	0.055	0.006	0.524	-2.520	0.012
Bagshaw 2010*	Mixed	1.563	0.933	2.619	1.697	0.090
Gettings 1999	Surgery	0.399	0.164	0.973	-2.019	0.043
Elahi 2004	Surgery	0.800	0.273	2.341	-0.407	0.684
Demirkilic 2004	Surgery	0.533	0.183	1.552	-1.154	0.249
Andrade 2007	Mixed	0.100	0.019	0.515	-2.752	0.006
Manche 2008	Surgery	0.051	0.010	0.256	-3.623	0.000
Iyem 2009	Surgery	0.778	0.229	2.644	-0.403	0.687
Shiao 2009	Surgery	0.260	0.110	0.614	-3.075	0.002
Bagshaw 2009 adj	Mixed	1.250	0.915	1.708	1.401	0.161
Wu 2007 adj	Surgical	0.259	0.068	0.988	-1.977	0.048
Carl 2010 adj	Mixed	0.380	0.177	0.816	-2.482	0.013
		0.446	0.276	0.723	-3.279	0.001



Meta Analysis

Karvellas et.al. Crit Care, 2011

Early (preemptive) vs Late (classic) : FINNAKI
-Prospective observational Finnish AKI study-

covariate	univariate Odds Ratio	p value	multivariate Odds Ratio	p value
Classic RRT (vs pre-emptive RRT)	2.25 (1.31 to 3.86)	0.003	2.05 (1.03 to 4.09)	0.04
Classic-delayed RRT (vs classic-urgent RRT)	3.37 (1.57 to 7.22)	0.002	3.58 (1.48 to 10.22)	0.01

Vaara ST et.al. CJASN, 2014

Summary (I)

- Fluid therapy is common in critically ill AKI patients
- There seems to be strong association between fluid overload and mortality
- Interstitial edema formation is likely to be the underlying mechanims of organ dysfunction by FO
- %FO is a newly introduced clinical parameter for the assessment of fluid overload in AKI patients, especially those receiving RRT

Summary (II)

- Published data do not convincingly demonstrate the superiority of one particular RRT modality with respect to fluid removal or mortality in critically ill patients

  Nevertheless, the use of conventional IHD remains problematic for many hemodynamically unstable AKI patients (reference KDIGO AKI Guideline) with diuretic resistance and severe fluid overload

- Optimal timing of RRT in fluid overload is not clearly defined

- Early initiation of RRT might be considered for maintaining fluid balance in critically ill patients with AKI

Thank you for your attention !

감사합니다.