Rationale for renal replacement therapy in ICU: indications, approaches and outcomes

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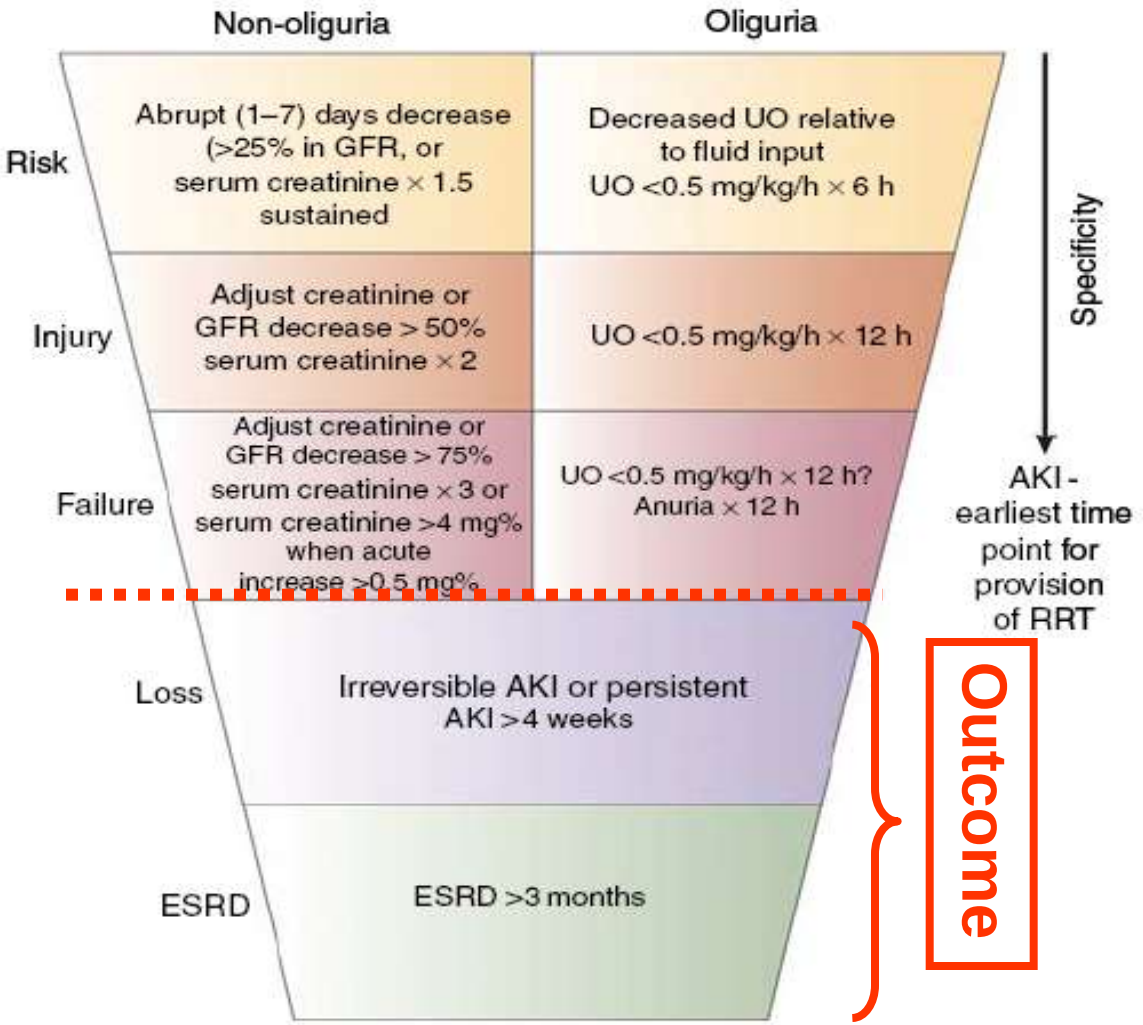
RIFLE classification (ADQI group) 2004



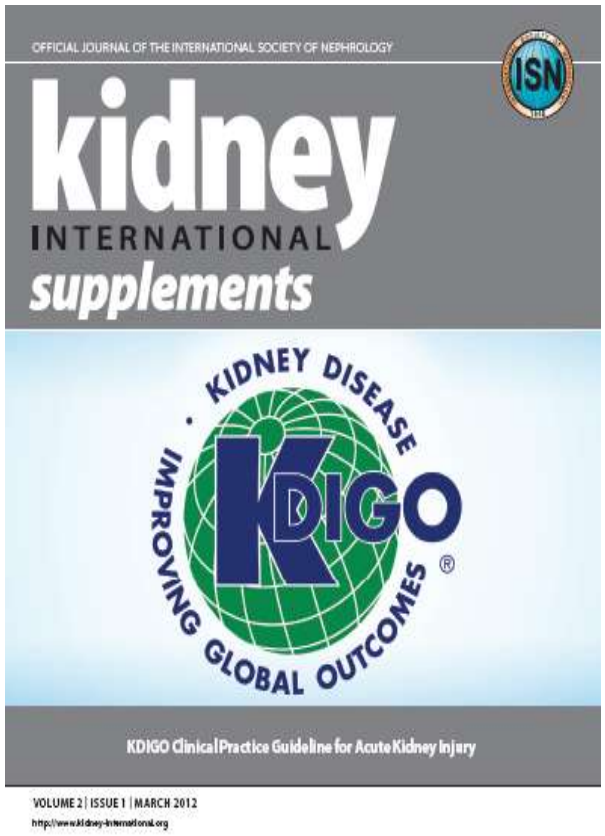
AKIN classification

Definition: Abrupt (**within 48 hrs**) change in serum creatinine or urine output (after exclusion of obstruction)

Stage	Creatinine criteria	Urine output
1	↑ serum creatinine of ≥0.3 mg/dl (26.4 µmol/L) or 1.5 – 2 fold increase from baseline	<0.5ml/kg/hr for > 6hr
2	2 – 3 fold rise of serum creatinine from baseline	<0.5ml/kg/hr for >12 hrs
3	> 3 fold rise of serum creatinine from baseline **or** serum creatinine ≥4.0 mg/dl (>354 umol/L) with an acute rise of at least 0.5 mg/dl (44 umol/L) **or** **treatment with RRT**	<0.3ml/kg/hr x 24hr or anuria x 12 hr

Mehta R et al. Crit Care 2007;11(2):R31

KDIGO classification



Aim:
To harmonise RIFLE and AKIN criteria and to agree on ONE universal definition

March 2012

KDIGO classification
Definition

We recommend that AKI be defined as any of the following (*1A*):

- **Increase in Scr by >0.3 mg/dl (>26.4 µmol/L) within 48 hours,**

  or

- **Increase in Scr by >1.5-fold above baseline which is known or presumed to have occurred within 7 days**

  or

- **Urine volume <0.5 ml/kg/h for 6 hours.**

KDIGO classification
Staging

If criteria for AKI met, we recommend to stage AKI as:

Stage	Serum Creatinine	Urine Output
1	≥ 1.5-1.9 times baseline or 0.3 mg/dl (>26.4 µmol/L) increase	< 0.5 ml/kg.h for ≥ 6-12 hrs
2	≥ 2.0-2.9 times baseline	< 0.5 ml/kg.h for ≥ 12 hrs
3	≥ 3.0 times baseline OR increase in creatinine ≥ 4 mg/dl (352 µmol/L) In patients < 18 yrs decrease of eGFR to 35 ml/kg/1.73 m^2	< 0.3 ml/kg.h for ≥ 24 hrs OR Anuria ≥ 12 hrs

RRT in AKI: Why?

RRT in AKI: Why?

Aims of RRT

- ✓ Amelioration of uraemia and fluid overload
- ✓ Metabolic homeostasis
- ✓ Volume homeostasis (ie. ARDS, CCF, MOF)

? Immunomodulation in sepsis

Replacement of renal function + organ support

Types of RRT in AKI

CRRT

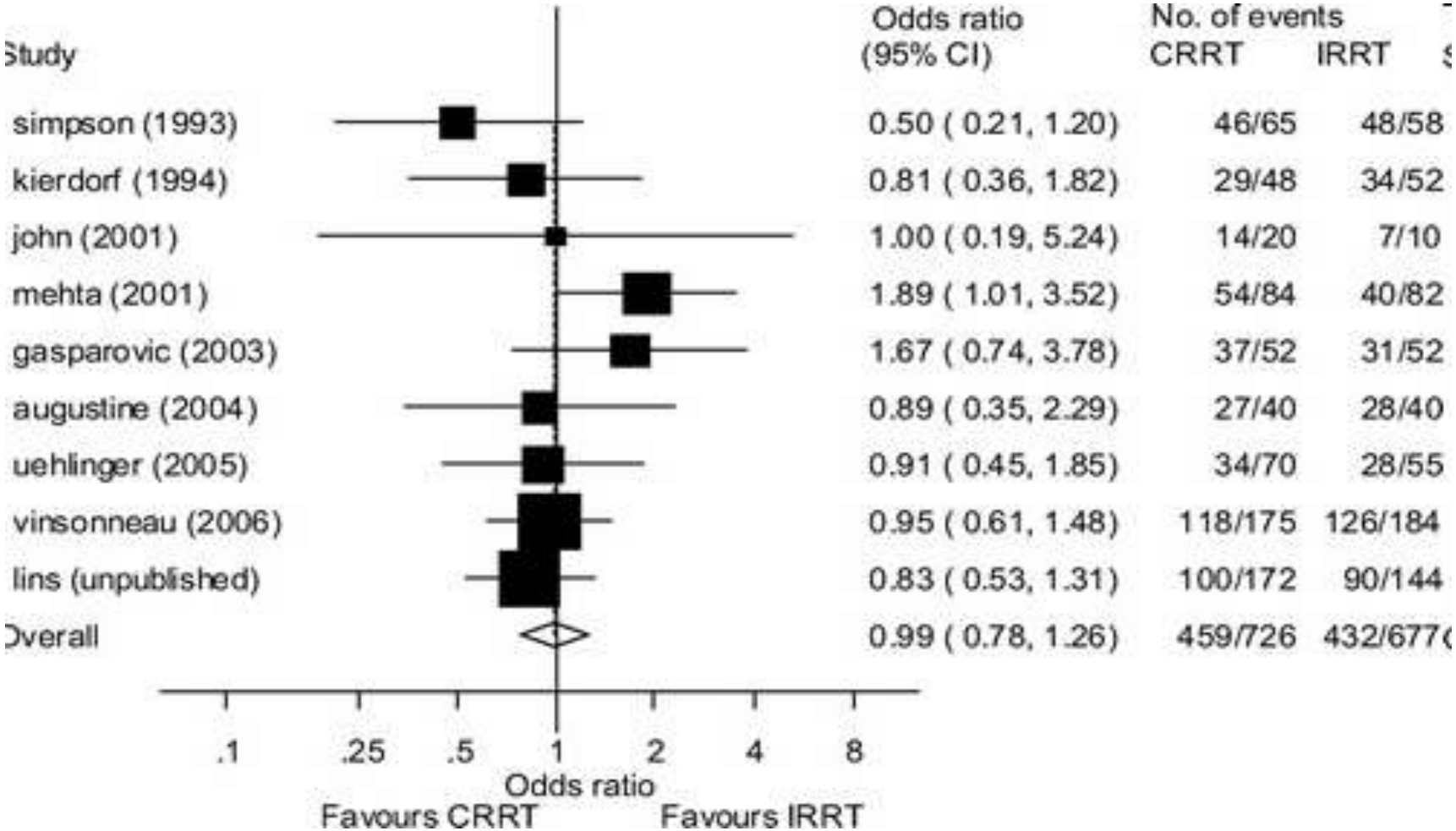
continuous veno-venous haemofiltration
continuous haemodialysis
continuous veno-venous haemodiafiltration
(peritoneal dialysis)

Intermittent RRT

intermittent haemodialysis
Slow Extended Dialysis (SLED)
Prolonged intermittent RRT (PIRRT)
SLED-F

Types of RRT in AKI

No evidence that CRRT is superior (patient survival, renal recovery)



Bagshaw SM et al. Crit Care Med 2008;36:610

CRRT or intermittent RRT ?

Advantages and disadvantages of both techniques

Aim: to identify optimal mode for individual patient

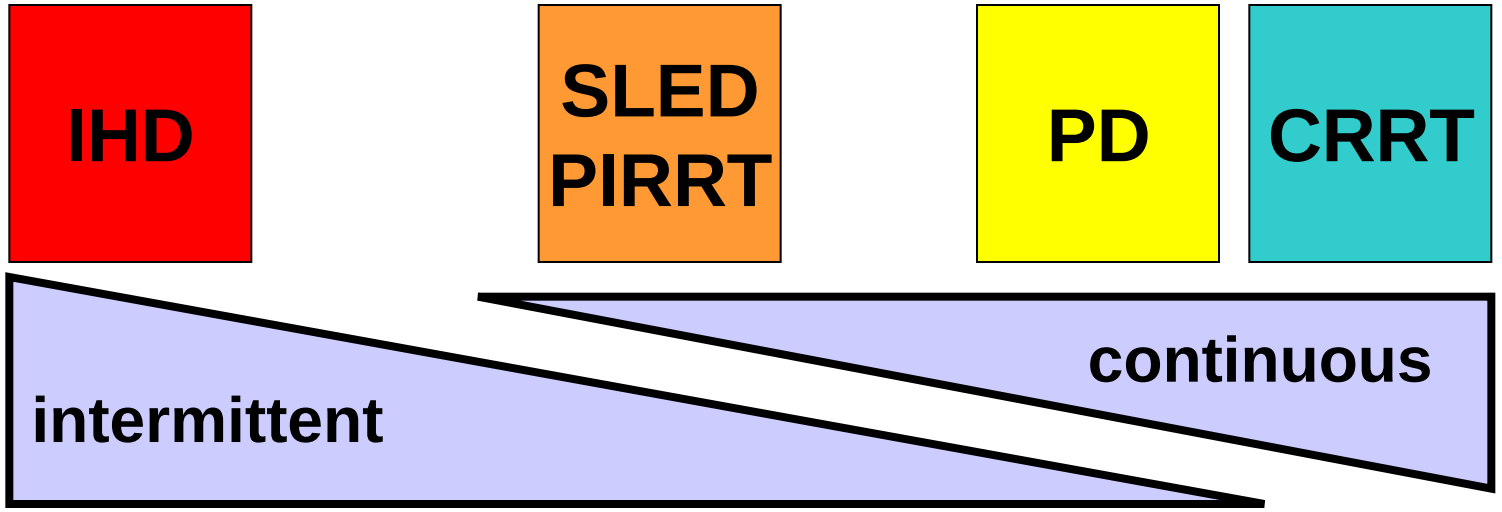
haemodynamic instability
severe fluid overload
brain oedema
liver failure

} **CRRT**

recovery phase
able to tolerate fluid swings

} **IHD / SLED / PIRRT**

Modality



Clearance per hour +++ ++

Fluid shifts

Changes in urea/NH_3/Na^+

RRT in AKI: When?

Optimal timing of RRT

Early RRT	Late RRT
Metabolic homeostasis Fluid management “easier”	Avoids RRT in patients whose renal function recovers without RRT Avoids potential complications of central line Cost saving Risk of uraemic complications

Optimal timing of RRT

No accepted definition of “optimal timing of RRT”

and wide variation in clinical practice

Variable interpretation of “optimal timing”:

? specific urea level
? specific creatinine level
? time since development of AKI
? time since admission to ICU
? time since admission to hospital

Optimal timing of RRT

Only 2 published RCTs (and 2 RCTs in abstract form) and at least 15 observational studies comparing

“early” vs “late” RRT

Optimal timing of RRT

Effects of early high-volume continuous venovenous hemofiltration on survival and recovery of renal function in intensive care patients with acute renal failure: A prospective, randomized trial

Catherine S. C. Bouman, MD; Heleen M. Oudemans-van Straaten, MD, PhD; Jan G. P. Tijssen, MD, PhD; Durk F. Zandstra, MD, PhD; Jozef Kesecioglu, MD, PhD

Crit Care Med 2002;30(10)

106 patients (3-organ failure, oliguric AKI)
1998 – 2000 ; 2-centre study

Randomisation:

	early high-volume CVVH	(72-96 L/24 hrs)
vs	early low-volume CVVH	(24-36 L/24 hrs)
vs	late low-volume CVVH	(24-36 L/24 hrs)

Optimal timing of RRT

Results:
No difference in 28-day survival
No difference in renal recovery

In the late low volume group:
2 patients died before criteria were met for late CVVH
4 patients had spontaneous recovery of renal function

Crit Care Med 2002;30(10)

Optimal timing of RRT

"Early start on continuous hemodialysis therapy improves survival rate in patients with acute renal failure following coronary bypass surgery"

28 patients post cardiac surgery

CRRT if urine output <30ml/h for 3 hours

vs

CRRT if urine output <20ml/h for 2 hours

Results:	14 day mortality	14%	(early CRRT)
		86%	(late CRRT)

Sugahara S et al. Hemodial Int 2004:8:320

Optimal timing of RRT

15 additional observational mainly retrospective studies

Early versus late RRT

First Author	Time period	RRT mode	n	Urea		Hospital mortality
Gettings	1989 - 1997	CAVHD CVVHD CVVH	100 trauma pts	<21 Day 10	≥21 Day 19	61% vs 80%
Tsai	2002 - 2005	CVVH IHD	98 post abdo Sx	23	27	43% vs 75%
Liu (PICARD)	1999 - 2001	CRRT IHD	243 mixed pts	<27	≥27	RR 1.85 with higher urea

Early versus late RRT

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Liu (PICARD)	1999 - 2001	CRRT IHD	243 mixed pts	<27	≥27	RR 1.85 with higher urea
Bagshaw (BEST)	2000 - 2001	CRRT IHD	1260 mixed pts	≤24	>24	No difference
				Creatinine		
				≤309	>309	71% vs 53.4%

Optimal timing of RRT

15 observational studies:

Most evidence in favour of “early” RRT stems from small retrospective observational studies.

But:

- inclusion of patients with AKI who would have recovered renal function anyway
- inclusion of patients into “late arm” who received RRT “too late”
- differences in severity of illness between groups

Parameters affecting mortality

Parameter at time of RRT	OR	p
Serum pH	0.03	<0.001
Age	1.03	<0.001
CVS failure	1.3	0.04
Urine output <400	1.6	<0.001
Respiratory failure	1.62	<0.001
Haematological failure	1.7	<0.01
Pre-existing advanced chronic illnesses	1.74	<0.001
Need for TPN	2.04	<0.001
Liver failure	2.44	0.001
Ventilated	6.03	<0.001
Serum Creatinine	0.999	
Serum Urea	1.004	

Ostermann et al, Crit Care 2009

Impact of fluid overload

"Fluid accumulation, survival and recovery of kidney function in critically ill patients with AKI"

PICARD study:
Observational study in 5 centres in California
1999 – 2001

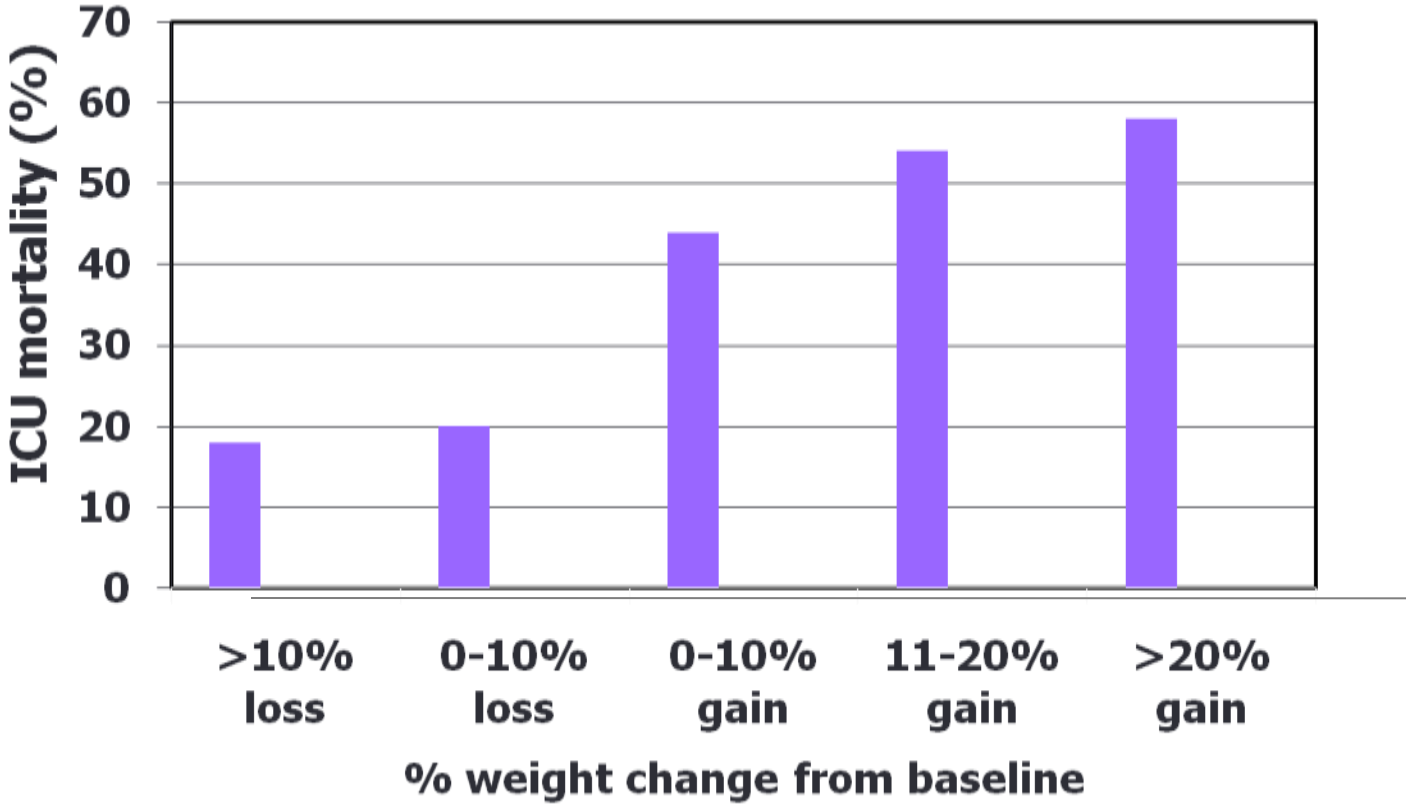
618 patients with AKI
of whom 398 patients received RRT (CVVH, CVVHD or IHD)

Fluid status defined as change from initial hospital admission weight.

Bouchard et al, KI 2009;76

Impact of fluid overload

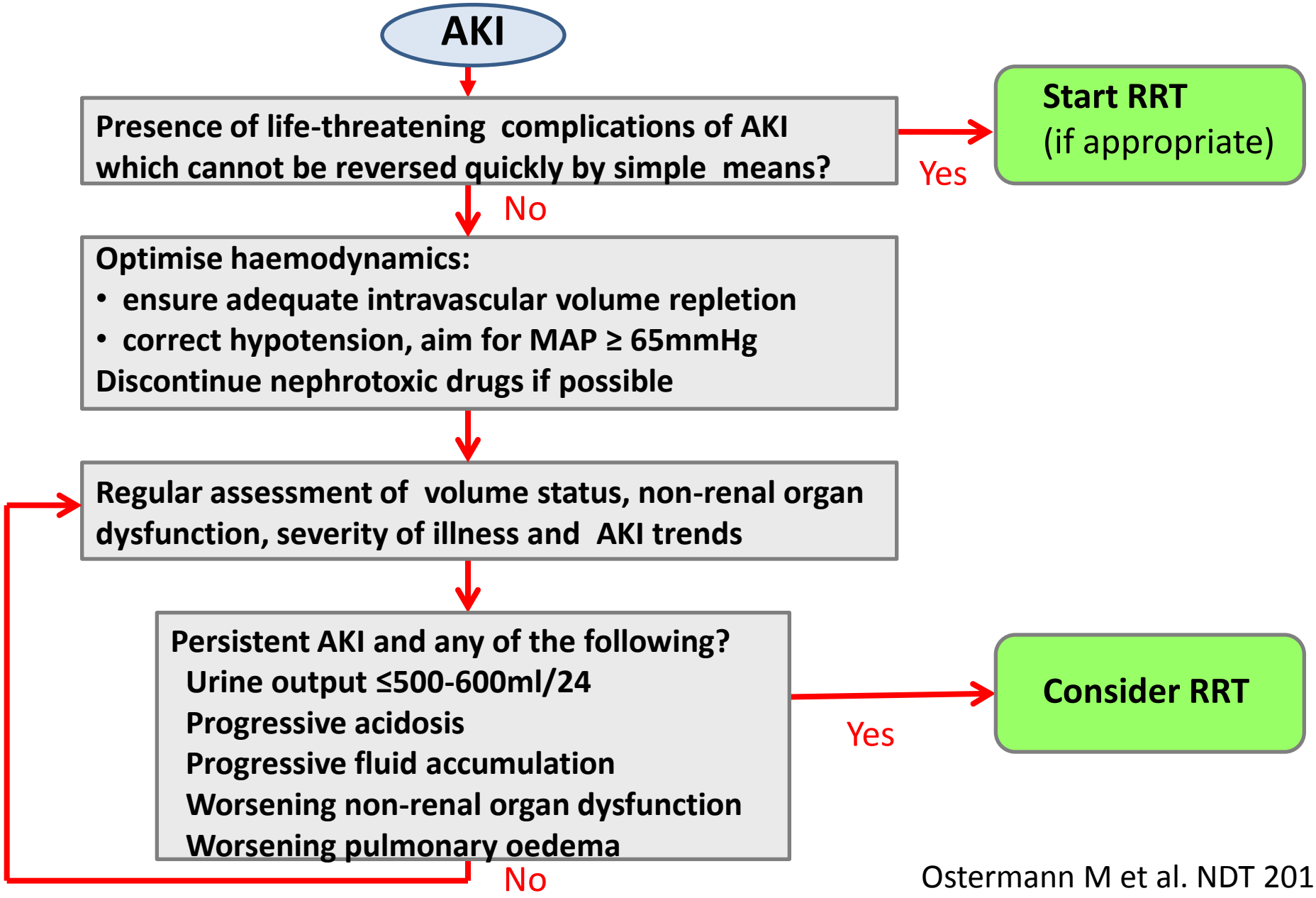
Mortality rate of RRT patients by final fluid accumulation relative to baseline weight



Bouchard et al, KI 2009;76

RRT in AKI: When?

RRT in AKI: When?



Ostermann M et al. NDT 2012

RRT in AKI: How much?

Dose of RRT

Traditional approach in ESRD: Kt/V

Kt/V not validated in AKI (lack of steady state, fluid shifts)

Measures of dose in RRT

1. Filtrate volume
2. Frequency of intermittent RRT

Optimal dose of RRT

"Effects of different doses in CVVH on outcomes of acute renal failure: a prospective randomised trial"

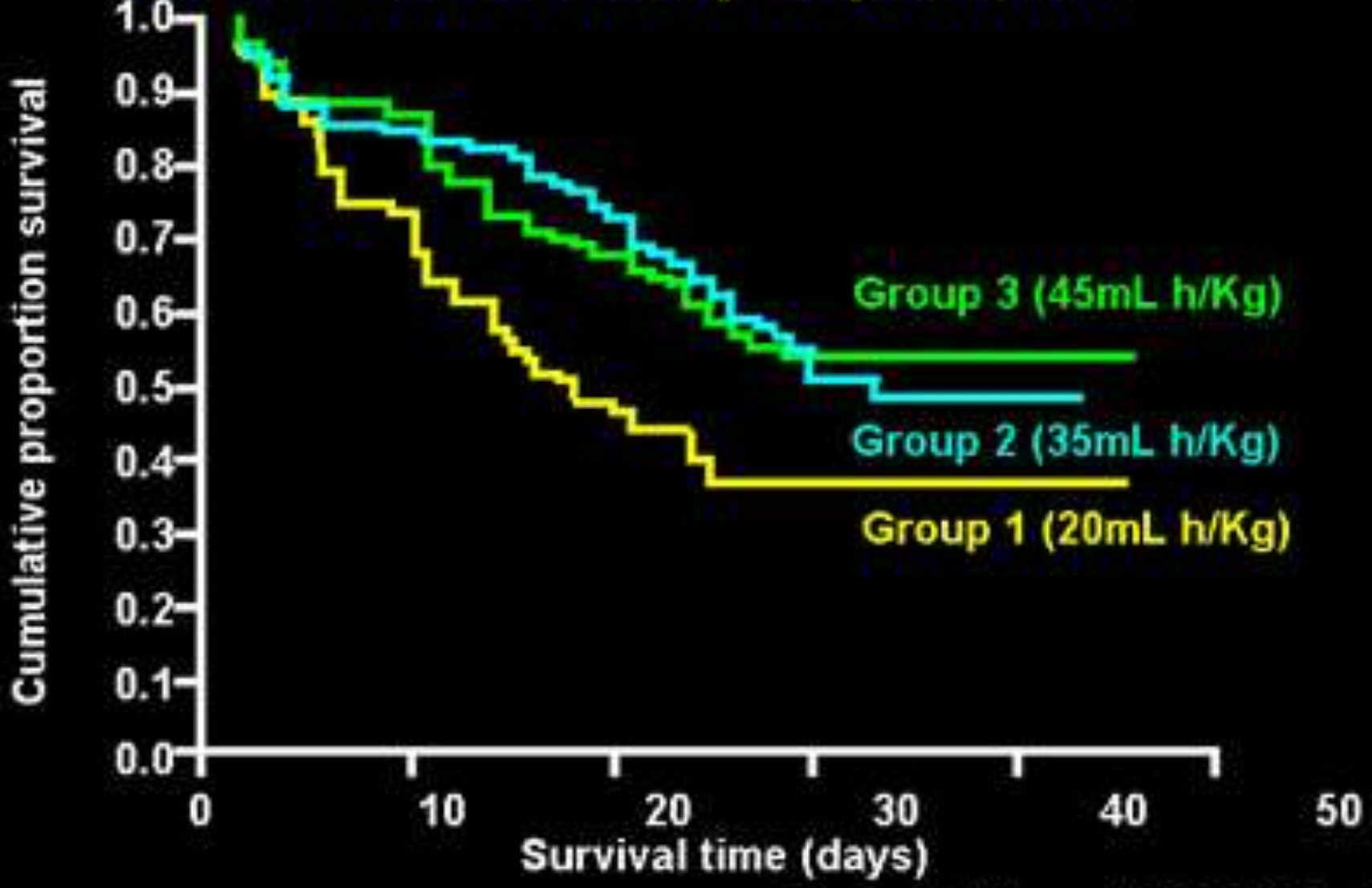
425 ICU patients with AKI

1994 – 1999

Protocol:	Group I:	UF 20 ml/kg/hr
	Group II:	UF 35 ml/kg/hr
	Group III:	UF 45 ml/kg/hr

Ronco et al, Lancet 2000;356

Effects of different doses of UF on outcome of ARF in critically ill patients.



Ronco et al, Lancet, 356, 26-30, 200

Optimal dose of RRT

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 3, 2008 VOL. 359 NO. 1

Intensity of Renal Support in Critically Ill Patients with Acute Kidney Injury

The VA/NIH Acute Renal Failure Trial Network*

Optimal dose of RRT

Intensity of Renal Support in Critically Ill Patients with Acute Kidney Injury

The VA/NIH Acute Renal Failure Trial Network*

1124 ICU patients with AKI and ≥1 non-renal organ failure or sepsis

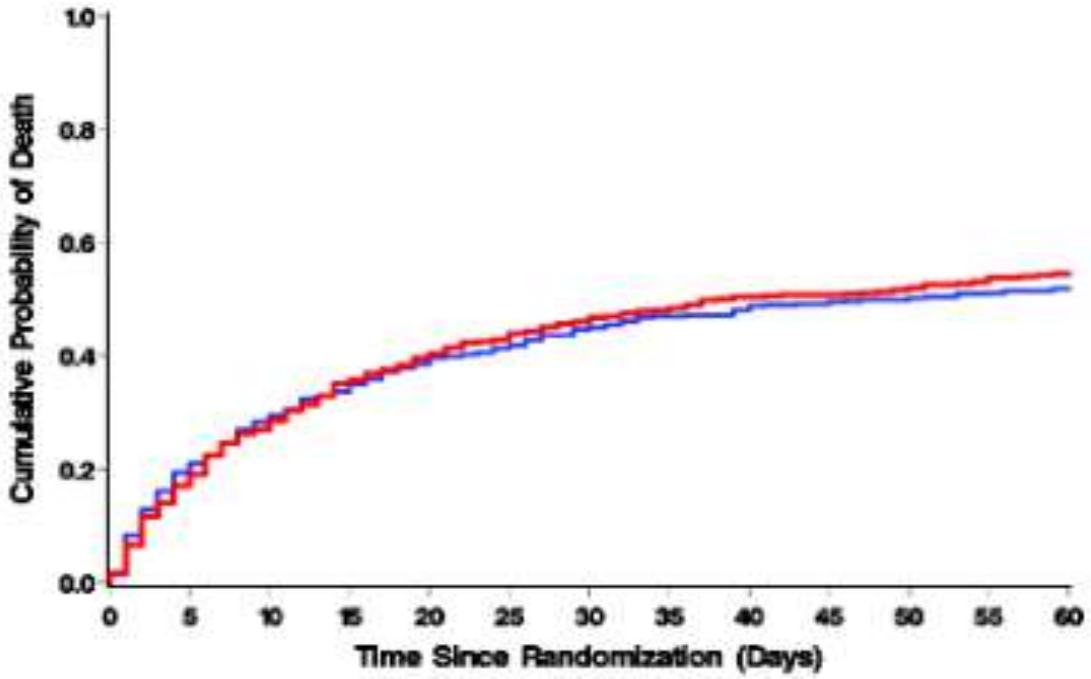
If haemodynamically stable: intermittent haemodialysis
3x / week or 6x / week

If haemodynamically unstable:

CVVHDF	or	SLED
20 ml/kg/hr vs 35 ml/kg/hr		3x/wk vs 6x/wk

Primary endpoint: 60 day mortality

Optimal dose of RRT



Conclusions:

Intensive renal support in critically ill patients with AKI did

not decrease mortality

not improve recovery of kidney function

not reduce the rate of non-renal organ failure

The VA/NIH Acute Renal Failure Trial Network. NEJM 2008;359

Optimal dose of RRT

Criticisms

1. No agreed criteria when to start RRT
2. Combined use of intermittent and continuous RRT
3. Modality switches within each treatment arm
4. Option of isolated ultrafiltration for volume management on non-dialysis days
5. Fixed dose of RRT throughout the dynamic course of AKI

The VA/NIH Acute Renal Failure Trial Network. NEJM 2008;359

Optimal dose of RRT

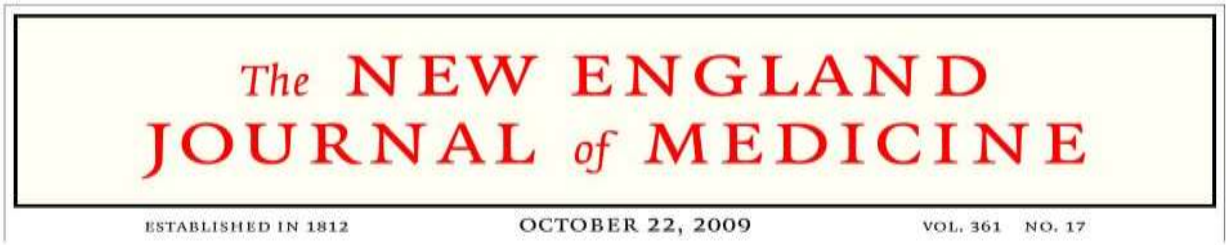
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 OCTOBER 22, 2009 VOL. 361 NO. 17

Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients

The RENAL Replacement Therapy Study Investigators*

Optimal dose of RRT



Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients

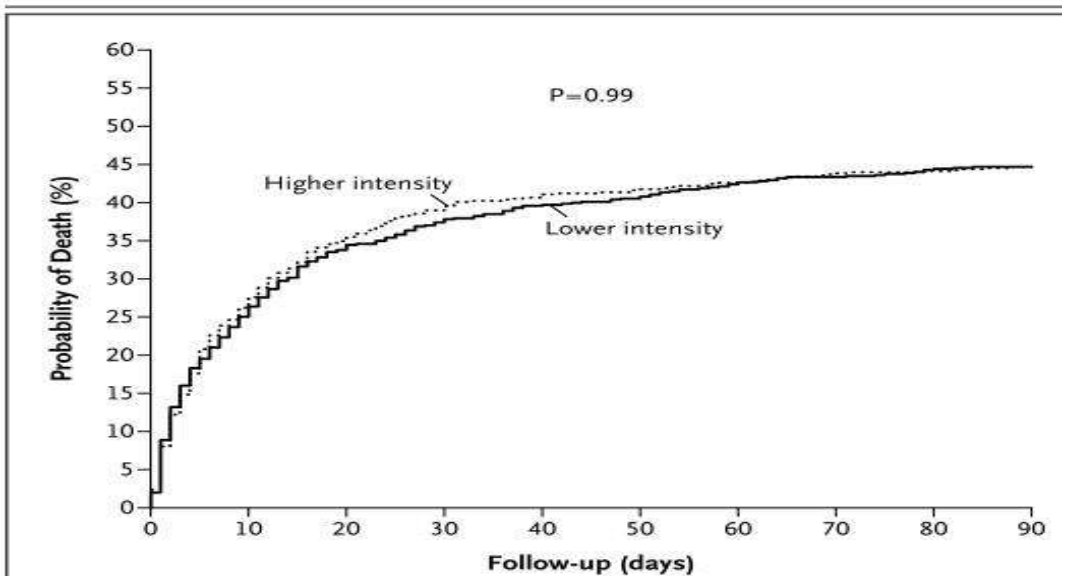
The RENAL Replacement Therapy Study Investigators*

1508 ICU patients with AKI

RCT : CVVHDF

40 ml/kg/hr (n=747) vs 25 ml/kg/hr (n=761)

Optimal dose of RRT



Conclusion:

Treatment with high dose RRT did not reduce 90 day mortality

RENAL study. NEJM 2009;361

Dose of RRT

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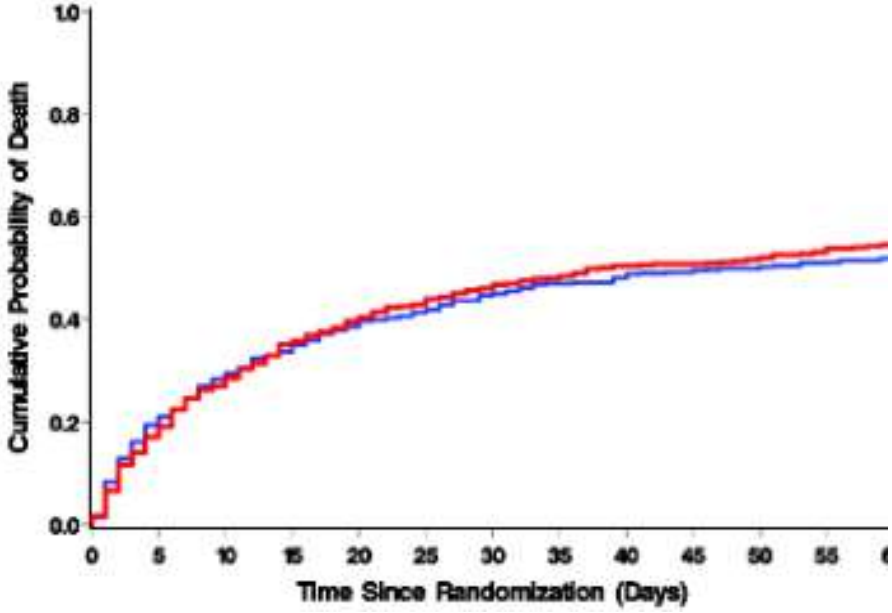

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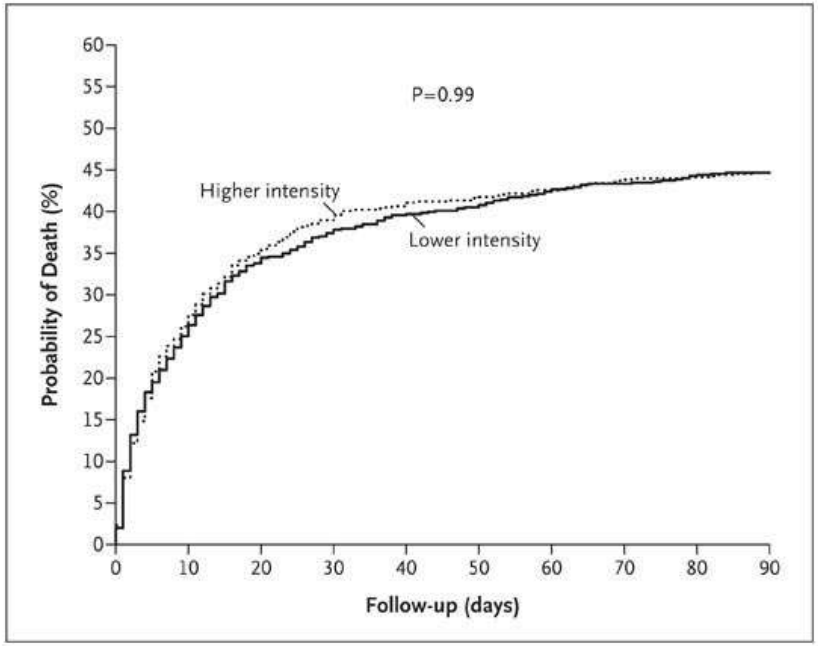
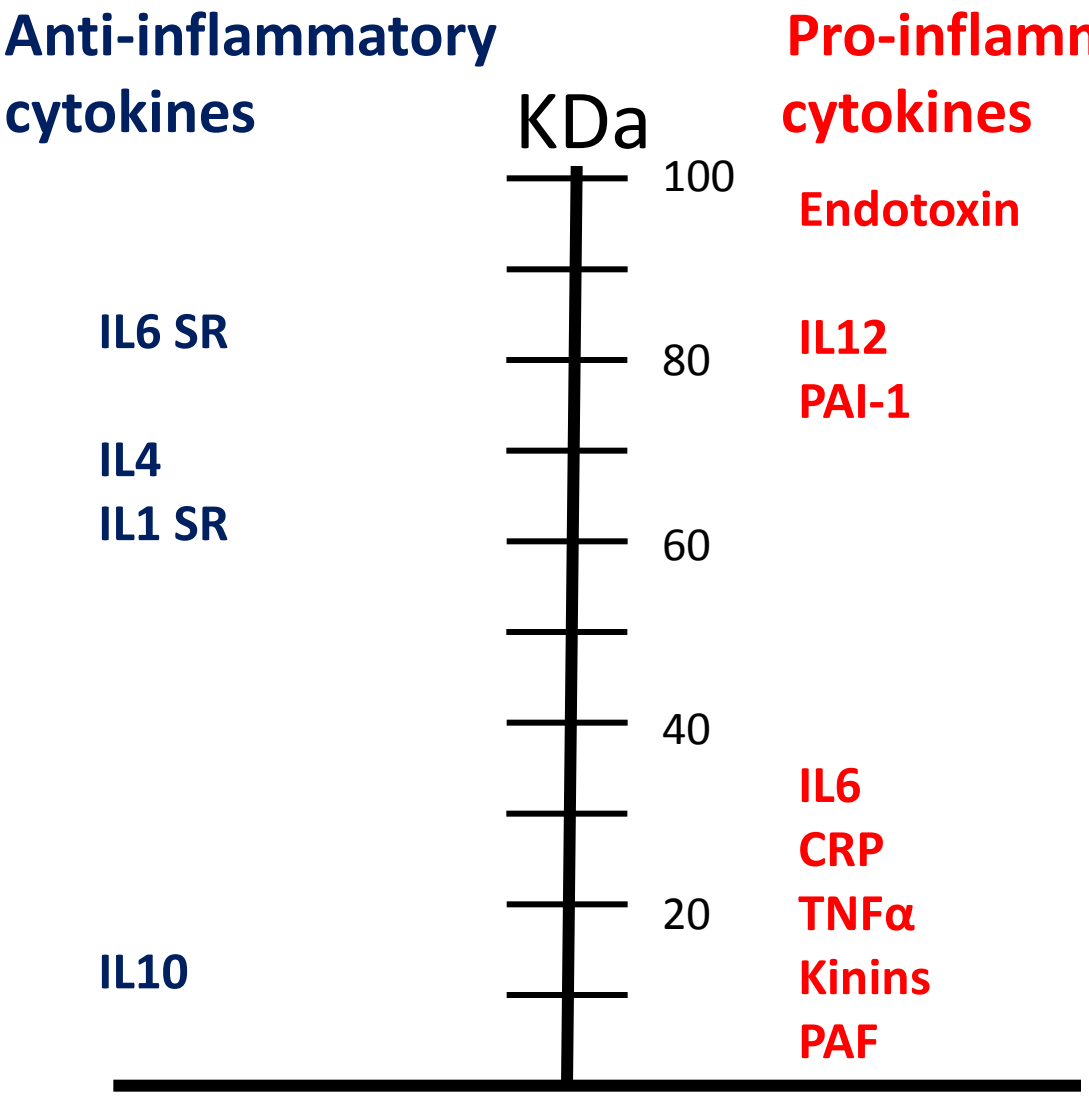


High dose RRT in sepsis / septic shock?

CRRT in sepsis



Membrane cut-off points

Polysulfone	30kDa
Polyamide	30kDa
AN69	50kDa
Polyamide100	100kDa

High dose RRT in sepsis / septic shock?

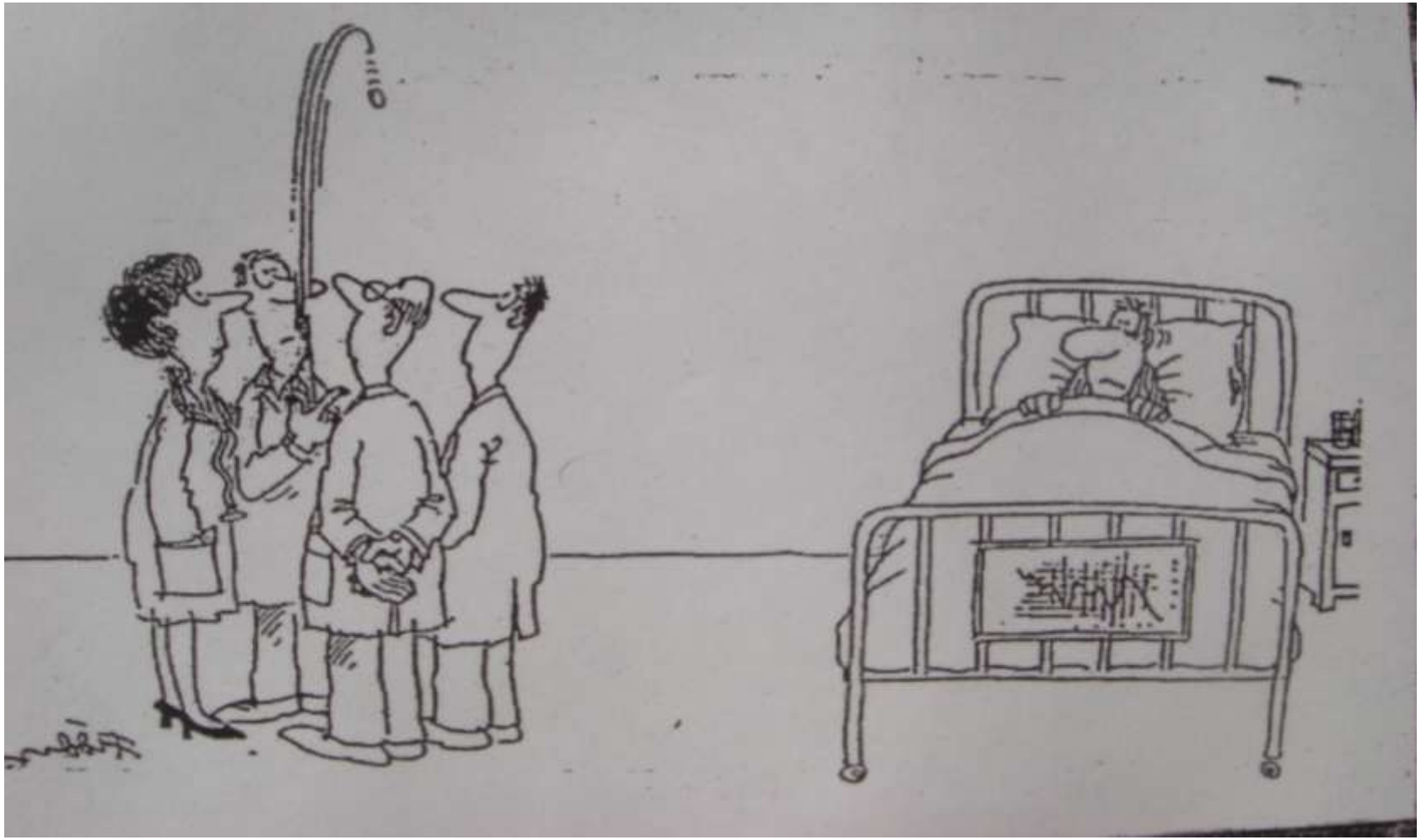
IVOIRE trial (HIgh VOlume in Intensive CaRE trial)

RCT: CVVH 70m/kg/hr vs CVVH 35ml/kg/hr
for 96 hrs

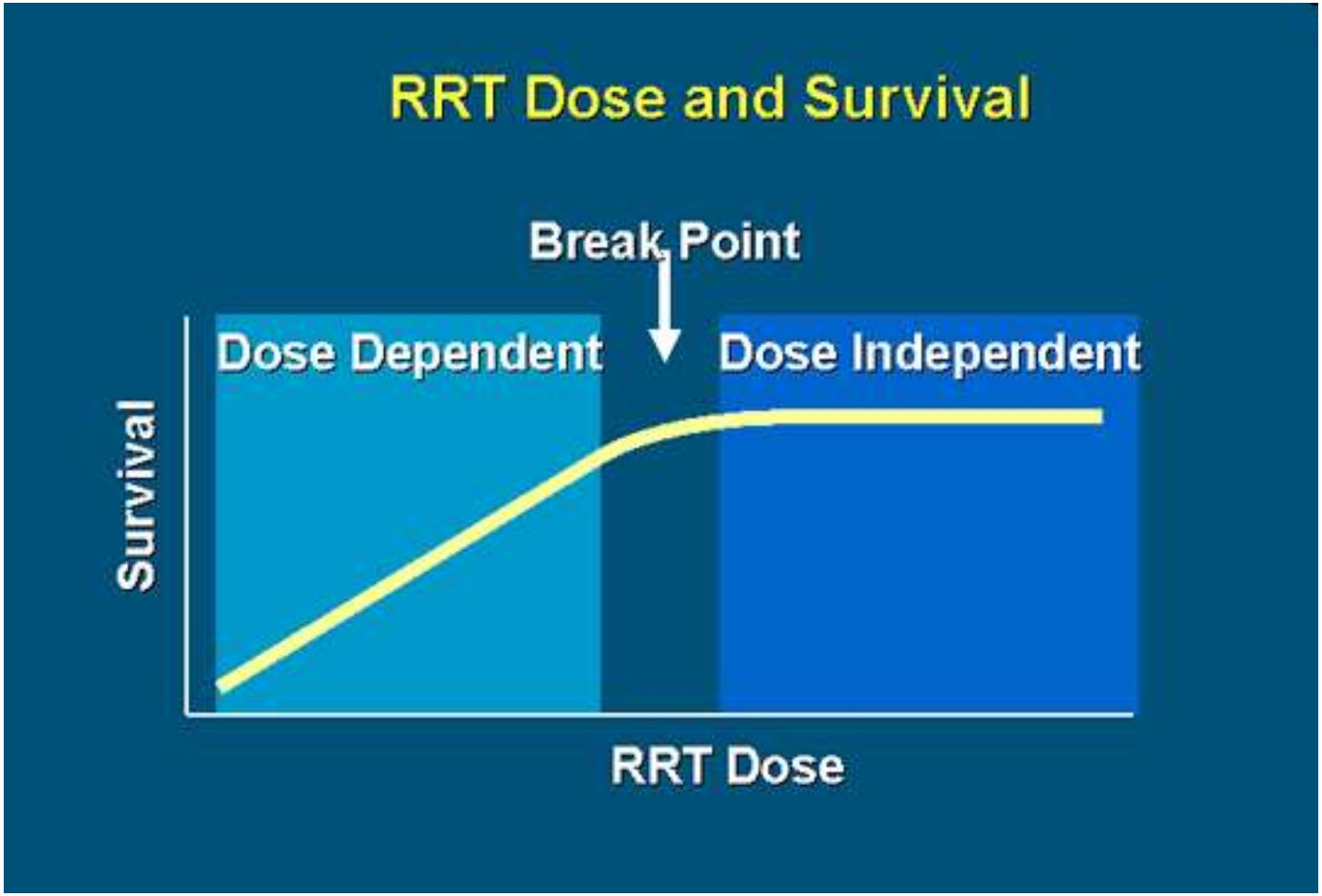
Planned study size: 460
Stopped in October 2010 after enrolment of 140 patients

Preliminary results:
No difference in 28 day mortality

Optimal dose of RRT



Optimal dose of RRT



Dose of RRT in daily clinical practice

"Delivered dose of renal replacement therapy and mortality in critically ill patients with AKI"

prospective multicenter observational study (8 countries)

419 pts on CRRT and 88 pts on intermittent RRT

Results:

- 20% of pts on CRRT had ≥1 interruption of 18hrs
- delivered dose of RRT often lower than intended as a result of treatment interruptions

Vesconi S et al. Crit Care 2009;13

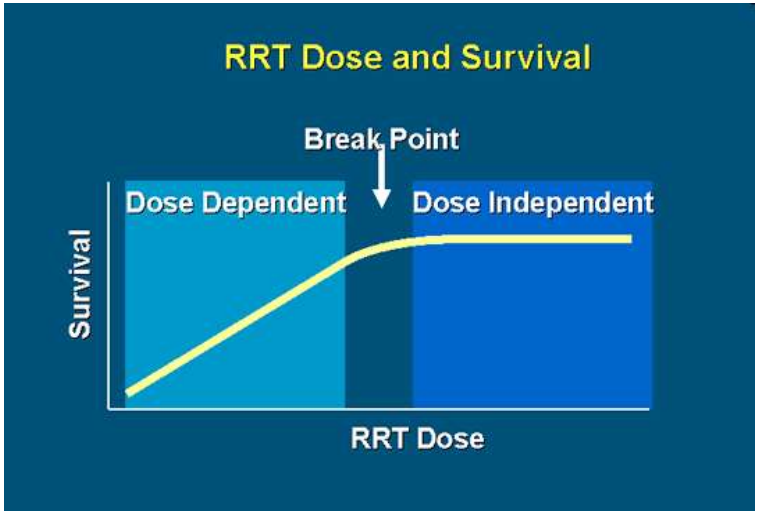
Dose of RRT in daily clinical practice

Reasons for treatment interruptions

- circuit clotting
- diagnostic and therapeutic procedures
- catheter malfunction

Vesconi S et al. Crit Care 2009;13

RRT in AKI: how much?



Consensus:

- There is no benefit in increasing the dose of RRT beyond a sufficient dose (~ 25ml/kg/hr)
- But: “Underdialysis” of critically ill patients must be avoided.
- Need for regular review and adjustment of RRT dose.
- Lack of data for flexible dosing (ie higher dose during acute phase)

Conclusions

Dialysis or CRRT?

No evidence that CRRT is superior to haemodialysis in AKI in most patients

But need for individualised treatment

Why?

to maintain homeostasis

to provide replacement of renal function and organ support

When?

AKI and progressive fluid accumulation, non-renal organ failure or metabolic acidosis, independent of creatinine

How much?

No evidence that “more” RRT is better than “enough”.

Consensus that 25ml/kg/hr adequate in most situations but undertreatment must be avoided

Need to review dose on regular basis and adjust Rx