Renal Replacement Therapy For Acutely Unwell Child

Loai Eid, MD, MSHS, FAAP
Consultant Pediatric Nephrologist
Pediatric Nephrology & Hypertension Division Chief
Dubai Hospital - DHA



Questions

- What therapy should we use?
- When should we start it?
- What are we trying to achieve?
- How much therapy is enough?
- When do we stop/switch?
- Can we improve outcomes?

Case

- 4 yo male admitted with gm negative septic shock. He is oliguric, 20% fluid overload, K of 6.8 meq/dl, Urea of 85 mg/dl, pH of 7.18. Intubated on 85% FIO2, Peep of 15. BP is 80/40 on 0.6 mic/kg/min of norepinephrine
- He needs RRT
- How?
- What will happen to his BP in dialysis ?

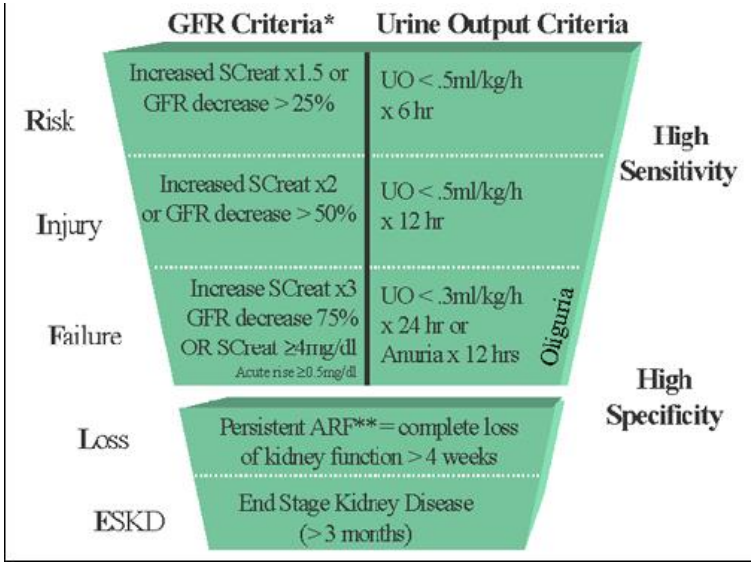
Pediatric AKI: Definition

Past: So many definitions….

Risk Injury Failure End-Stage Kidney Disease (RIFLE)

Pediatric RIFLE (pRIFLE)

Acute Kidney Injury Network definition



Crit Care. 2005; 9(5): 523–527

Table 6 | Pediatric-modified RIFLE (pRIFLE) criteria

	Estimated CCl	Urine output
Risk	eCCl decrease by 25%	<0.5 ml/kg/h for 8 h
Injury	eCCl decrease by 50%	<0.5 ml/kg/h for 16 h
Failure	eCCl decrease by 75% or eCCl <35 ml/min/1.73 m^2	<0.3 ml/kg/h for 24 h or anuric for 12 h
Loss	Persistent failure >4 weeks	
End stage	End-stage renal disease (persistent failure >3 months)	

eCCl, estimated creatinine clearance; pRIFLE, pediatric risk, injury, failure, loss and end-stage renal disease.

Kidney International (2007) **71,** 1028–1035.

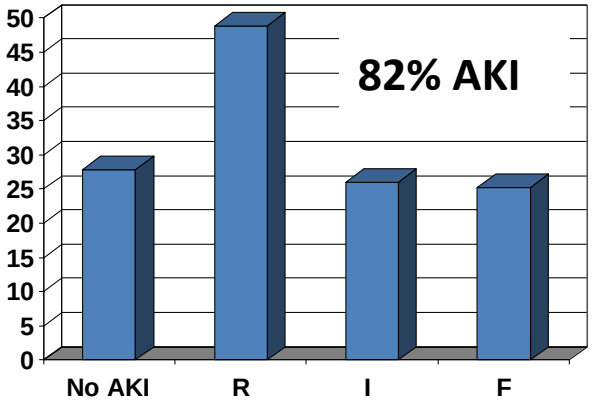
Pediatric AKI: Incidence in PICU Population & Definition-dependent

Most Critically ill children
Vasopressors/Ventilated
Urinary catheter

N=395

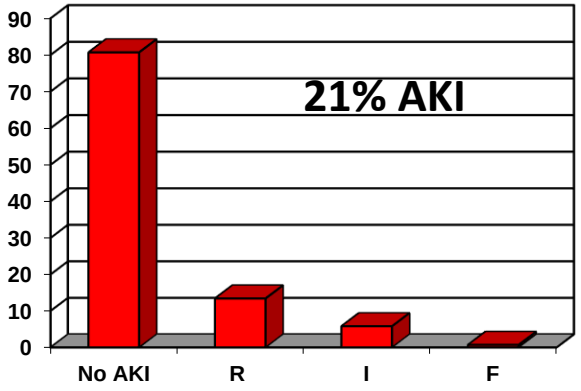
All PICU stay>48hrs

pRIFLE



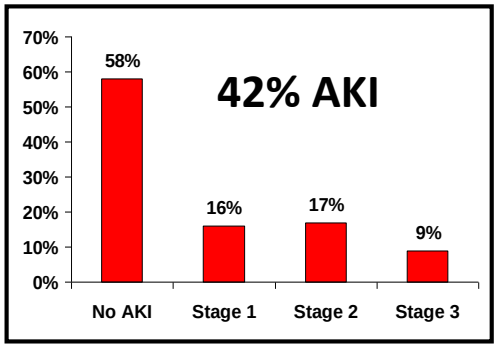
Kid Int 2007; 71: 1028-35

Cardiac Surgery



Anesth Analg 2009;109:45–52
(Aprotinin study)

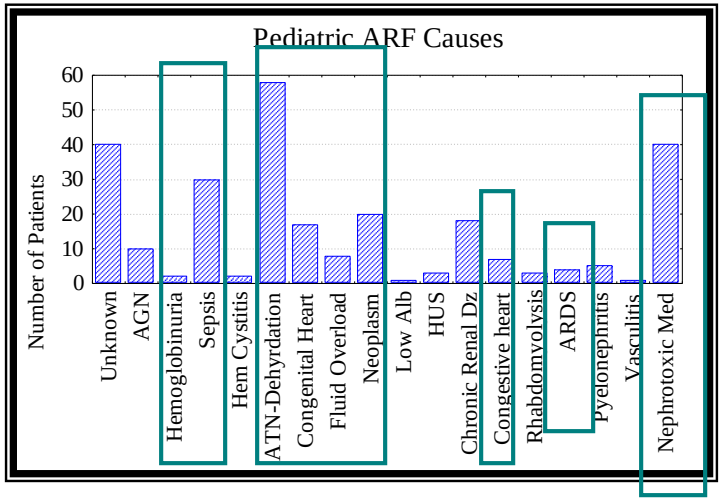
pRIFLE



Al-Kandari et al, ASN, 2008

Pediatric AKI:
Changing Epidemiology

Previously: Primary renal diseases



Stickle SH et al: Am J Kid Dis 45:96-101, 2005

Table 4. Characteristics and outcome of the acute renal failure (ARF) cases (n = 44)

Etiologies of ARF	
HUS	8 (18.2)
Hematology: oncology pathologies	8 (18.2)
Cardiac surgery	5 (11.4)
Sepsis	4 (9.1)
Trauma	3 (6.8)
Diabetic ketoacidosis	3 (6.8)
Chronic renal failure	3 (6.8)
Others	10 (22.7)

Pediatr Crit Care Med 2007 Vol. 8, No. 1

Pediatr Nephrol (2009) 24:1379–1384

Table 2 Causes of acute kidney injury

Cause	Numbers and percentages=100
Bone marrow transplantation related	27
Primary renal disease	14
Dehydration	10
Nephrotoxic medication	8
After cardiac surgery	8
Congenital anomalies of the urinary tract	2
Multiple etiologic factors with underlying chronic diseases	31
Total	100

Pediatric Patient with AKI: *Characteristics*

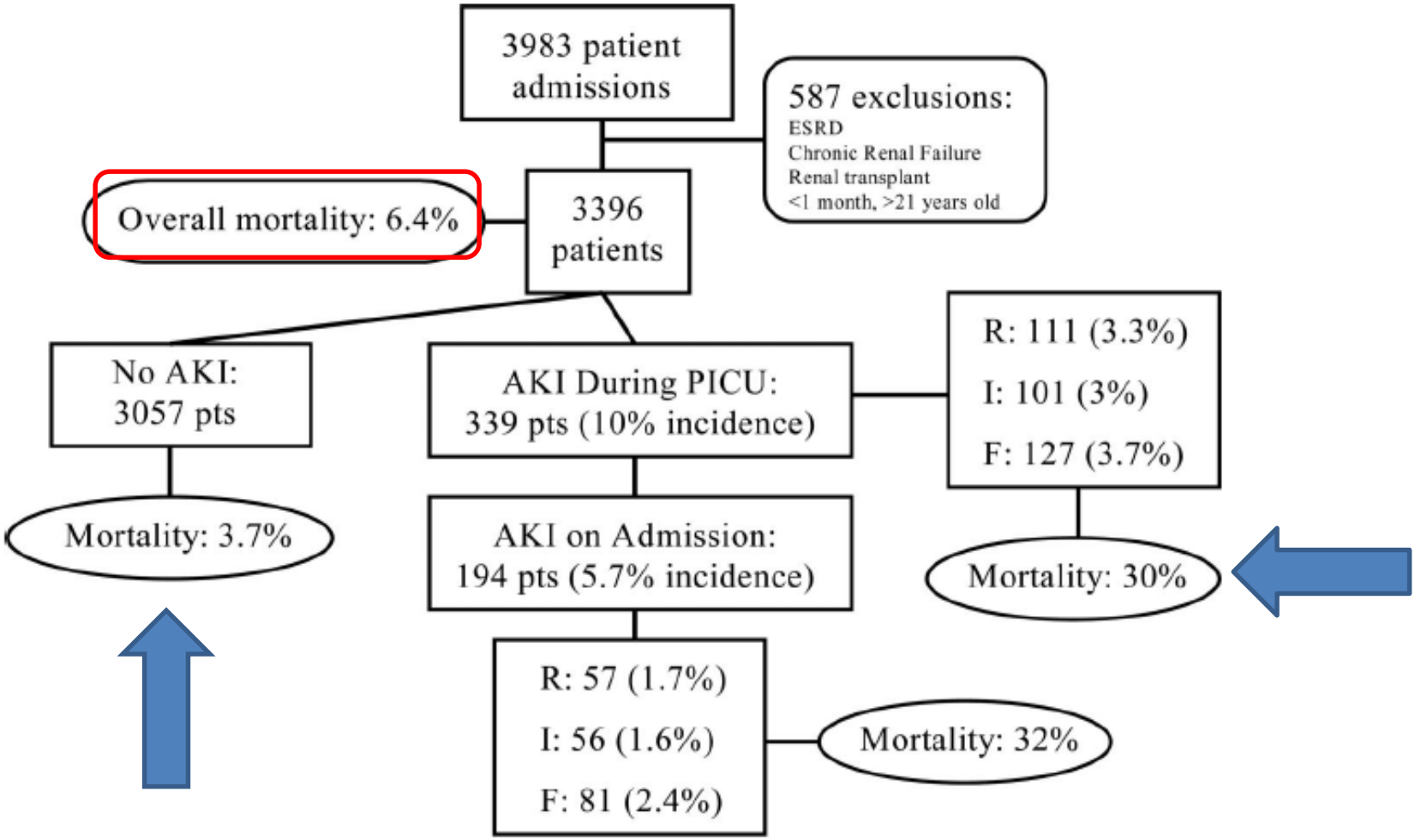
- **Children are NOT small adults**
  - 0 days to 18+ years
  - 2 kg to 100 kg
- **Primary conditions**
  - Congenital heart disease
  - Inborn errors of metabolism
  - Sepsis with multi-organ involvement
  - Bone marrow and solid organ transplantation
  - NOT RENAL
- **Children develop MODS early in ICU course**
  - Maximum number of organ failures occurs within 72 hours of ICU admission (87% of patients)
- **Children die with MODS very early in ICU course**
  - 88.4% of deaths occur within 7 days of MOSF diagnosis

Care Med 22:1025, 1994

Serum creatinine as stratified in the RIFLE score for acute kidney injury is associated with mortality and length of stay for children in the pediatric intensive care unit

Crit Care Med 2010 Vol. 38, No. 3

James Schneider, MD; Robinder Khemani, MD; Carl Grushkin, MD; Robert Bart, MD



Clinical Issues in AKI

- **Oliguria:**

– Volume overload and hypertension

– Inability to provide nutrition, therapy

- **Diminished renal clearance:**

– Electrolyte imbalance

– Acidosis

– Uremia

Conservative Management of AKI: Traditional Methods

- **Limit fluid intake**

– Can reduce volume overload problems
– Can't address issues of nutrition

- **Limit input of retained substances**

– Can reduce risks for hyperkalemia
– Can't address imbalances from metabolism

- **Adjustment of drug dosages in AKI**

- **Try not to mess up; wait and Hope**

Do Diuretics Help in AKI?

Table 1. Summary of non-randomized studies of loop diuretics in acute kidney injury

Study, First Author (Reference No.)	Year	No. Patients	Loop Diuretics Protocol	Toxicity	Comment
Beroniade (61)	1969	24	Furosemide, 60–480 mg	None reported	Not ICU
Cantarovich (66)	1973	105	Furosemide, 100–3200 mg IV, fixed/progressive daily	None reported	Not ICU Anuric for >2 days before enrollment All on RRT at enrollment
Chandra (69)	1975	28	Furosemide, 200–2000 mg IV, fixed/progressive daily	Deafness (n = 2)	Not ICU Oligo-anuric for >5 days before enrollment
Minuth (74)	1976	40	Furosemide, 250–500 mg IV	None reported	Not all ICU
Borirakchanyavat (62)	1979	14	Furosemide, 2000 mg IV daily	None reported	Not all ICU No patient died or needed RRT
Lumlertgul (73)	1989	23	Furosemide, 200 mg IV every 6 hrs	None reported	Not all ICU Co-intervention (DA) No patient died
Mehta (44)	2002	552	80 mg (20–320)[a]	None reported	Secondary question of study
Uchino (45)	2004	1743	240 mg (80–500)[b]	None reported	Secondary question of study

IV, intravenous; DA, dopamine; RRT, renal replacement therapy; ICU, intensive care unit.
[a]Median (intraquartile range) dose before consultation with nephrologist; [b]median (intraquartile range) dose in 24 hrs before enrollment.

8 non-randomized studies

Table 2. Summary of randomized studies of loop diuretics in acute kidney injury

Study First Author (Reference No.)	Year	No. Patients	Loop Diuretics Protocol	Toxicity	Comment
Cantarovich (65)	1971	47	Furosemide, 100–3200 mg IV fixed/progressive daily	Tinnitus[a]	All on RRT at enrollment
Karayannopoulos (70)	1974	20	Furosemide, 1000–3000 mg IV daily	None reported	Not ICU
Kleinknecht (71)	1976	66	Furosemide, 3 mg/kg IV load, 1.5–6.0 mg/kg IV every 4 hrs	Tinnitus, deafness, vertigo[a]	Not ICU Co-intervention (MA) Most already on RRT
Brown (63)	1981	53	Furosemide, 3 mg/kg IV load, 1–3 mg every 8 hrs orally	Deafness (n = 2)	Not ICU Furosemide given to both
Shilliday (76)	1997	92	Furosemide or torsemide, 3 mg/kg IV every 6 hrs	Deafness (n = 1)	Co-interventions (DA, MA)
Cantarovich (67)	2004	330	Furosemide, 25 mg·kg^{-1}·day^{-1} IV or 35 mg·kg^{-1}·day^{-1} orally	Deafness (n = 4)	All on RRT at enrollment

IV, intravenous; RRT, renal replacement therapy; ICU, intensive care unit; DA, dopamine; MA, mannitol.
[a]Estimates of occurrence of toxic effect were not reported. In these studies, ototoxicity may have been confounded by concomitant use of aminoglycosides. Symptoms were reported to occur temporally within a few hours after furosemide administration. No long-term sequelae were reported.

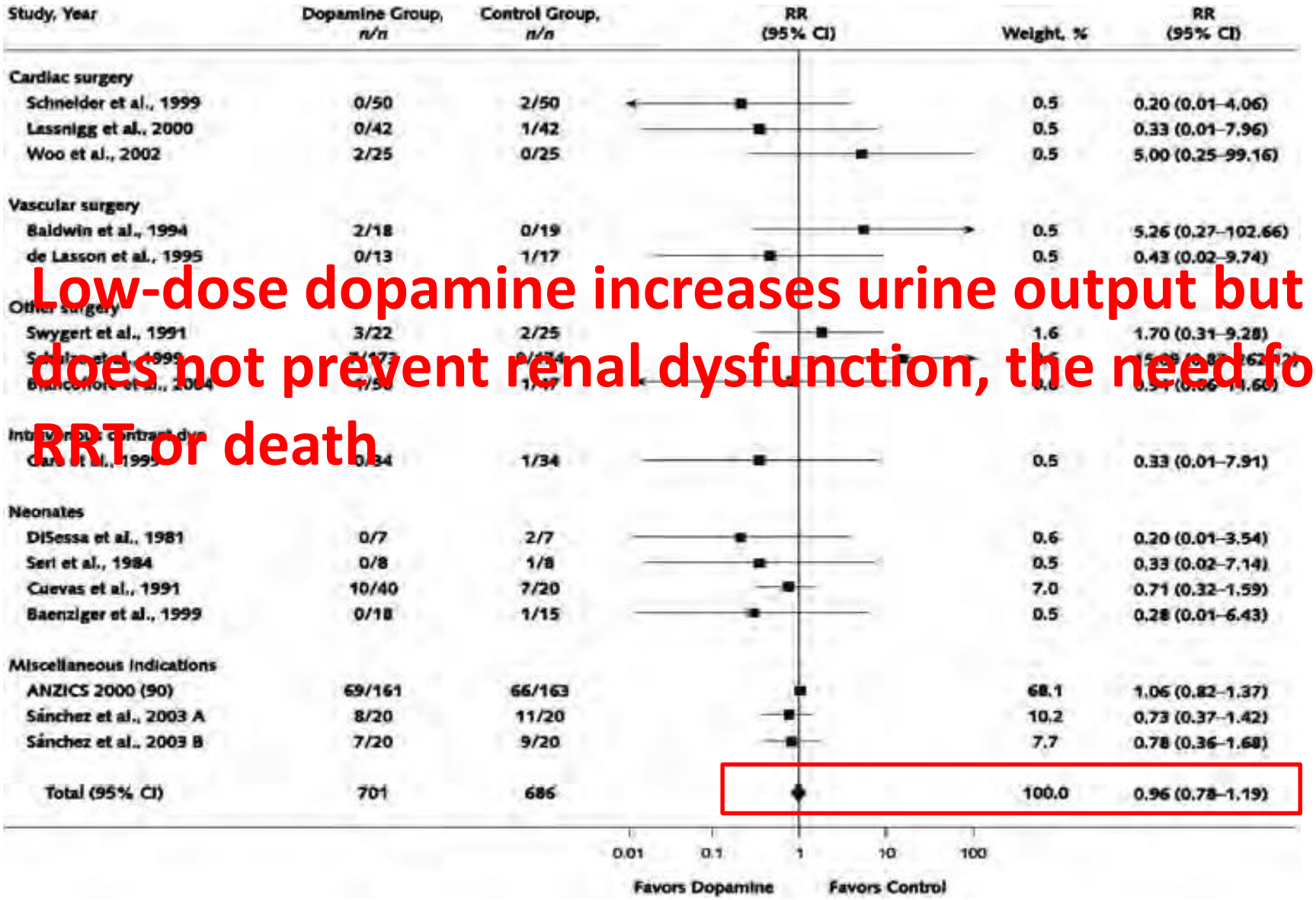
6 randomized studies

1. Majority of ICU patients get diuretics

2. ***But*** no improvement in clinical outcomes

Bagshaw CCM 2008 36(4)

Effect of Low-Dose Dopamine on Mortality



Low-dose dopamine increases urine output but does not prevent renal dysfunction, the need for RRT or death

Friedrich JO, Adhikari N, Herridge MS et al. Ann Intern Med 2005; 142: 510–524

Renal Replacement Therapy

Indications

- Volume overload
- Metabolic imbalance
- Toxins (endogenous or exogenous)
- Inability to provide needed daily fluids due to insufficient urinary excretion

Goals

- Restore fluid, electrolyte and metabolic balance
- Remove endogenous or exogenous toxins as rapidly as possible
- Permit needed therapy and nutrition
- Limit complications

RRT Options in AKI

- **Hemodialysis, Peritoneal Dialysis, & CRRT**

– Each has advantages & disadvantages

- **Modality Choice guided by**

1) Patient Characteristics

- Disease/Symptoms
- Hemodynamic stability

2) Goals of therapy

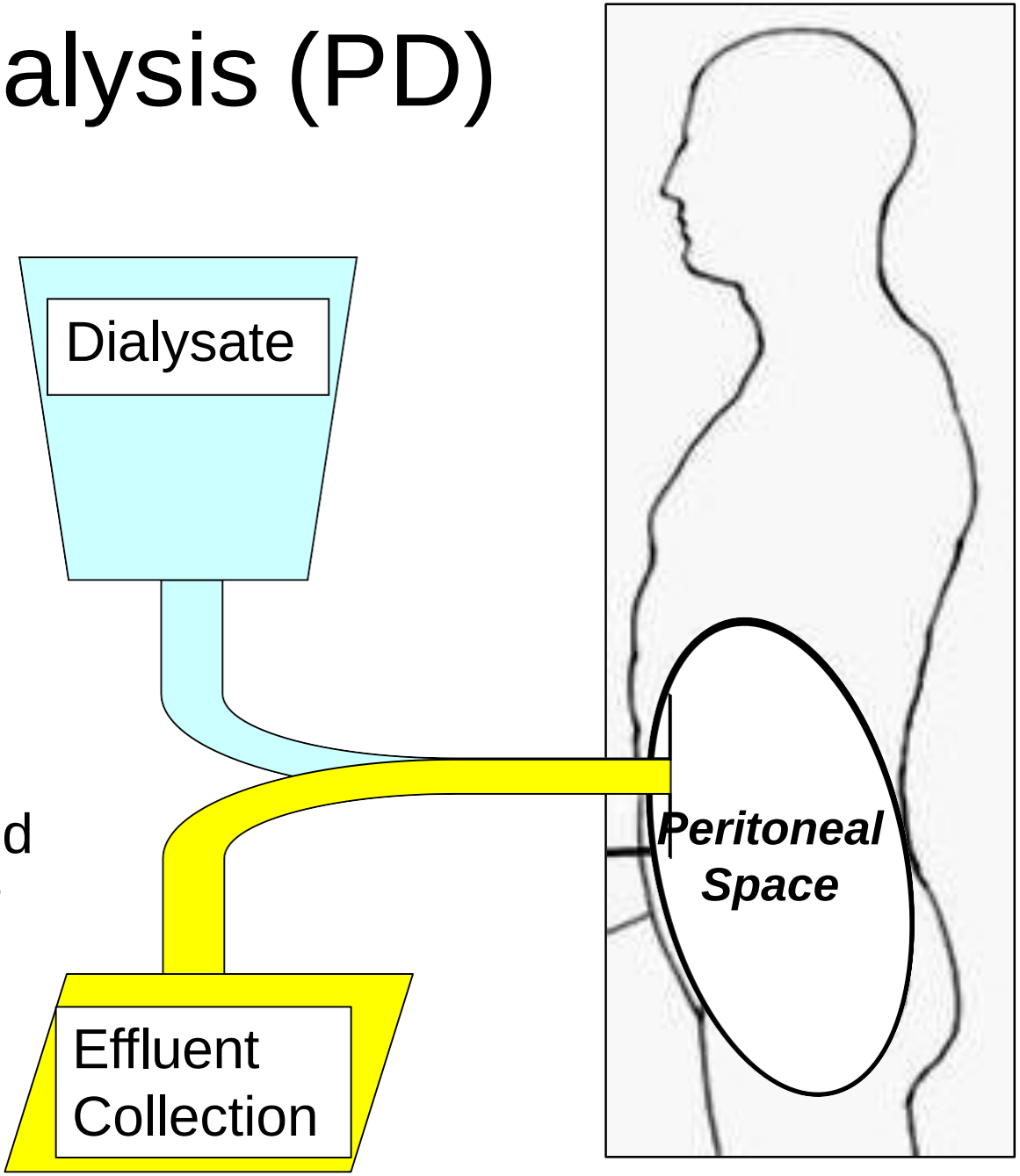
- Fluid removal, electrolyte correction, or both

3) Availability, expertise and cost

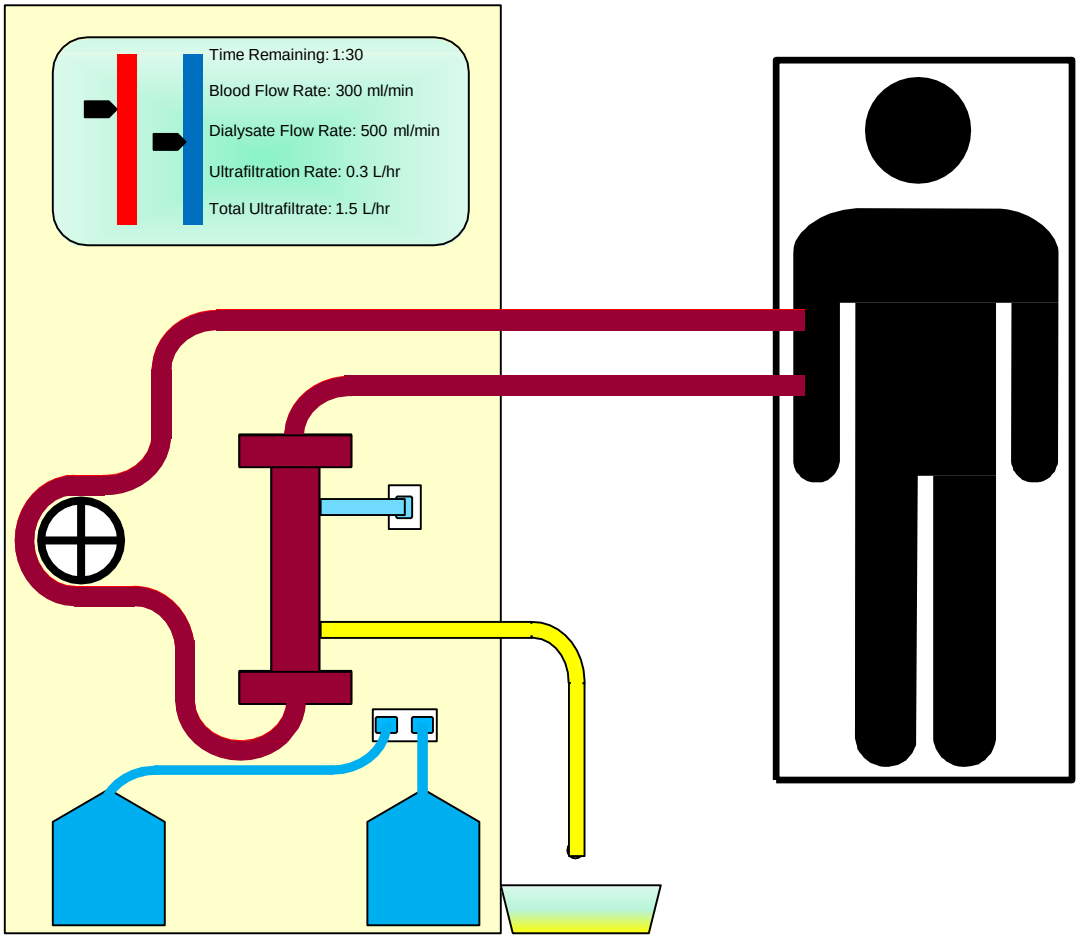
Walters et. al. Pediatr Nephrol 2008

Peritoneal Dialysis (PD)

- Sterile dialysate introduced into peritoneal cavity through a catheter
- Lots of pediatric experience
- Low efficiency system, variable UF
- Possibly better tolerated by critically ill patients?
- Often preferred in infants, especially with congenital heart dz

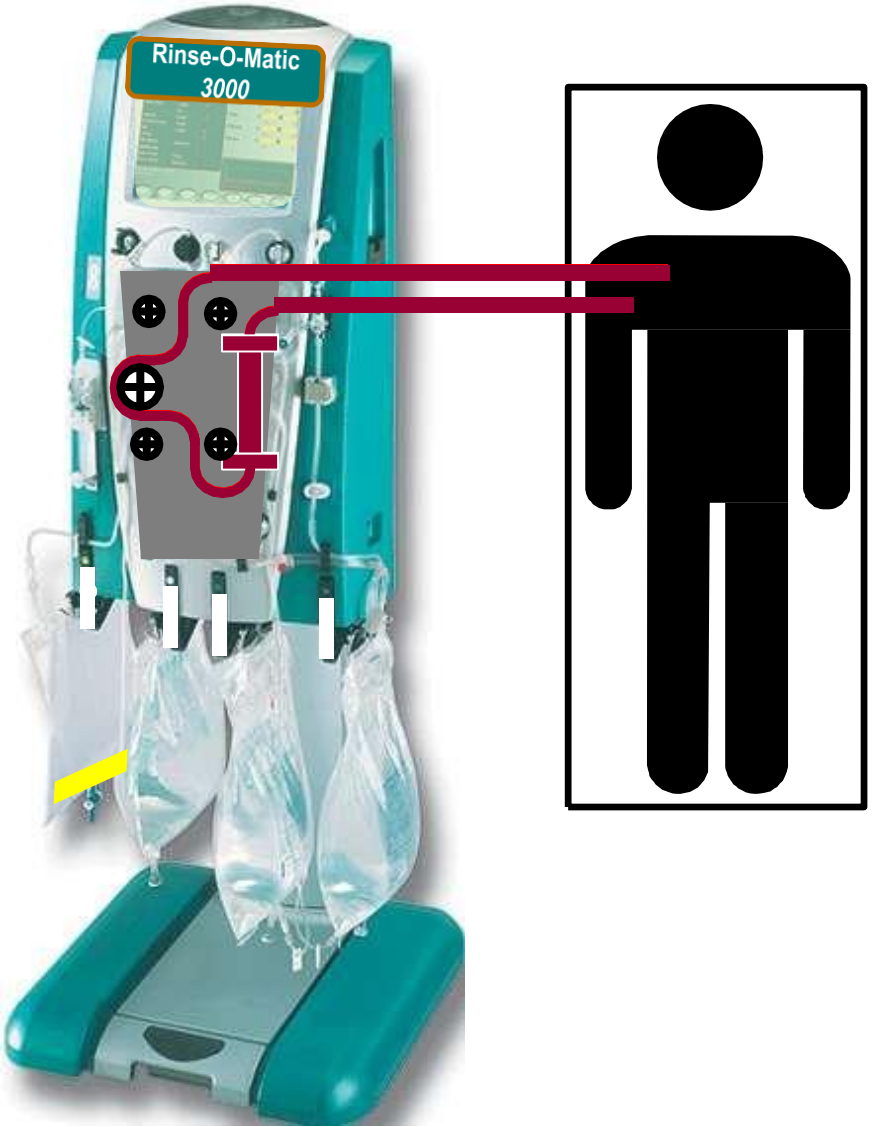


Intermittent Hemodialysis (IHD)



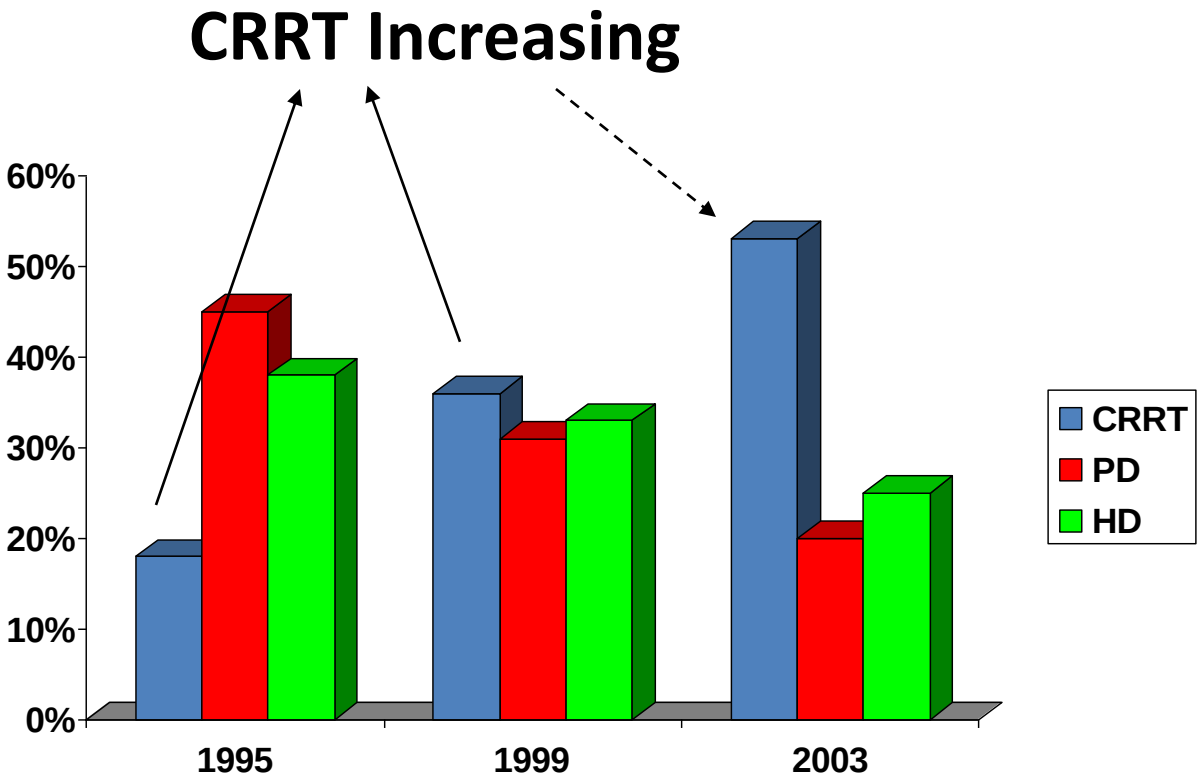
- Blood perfuses extracorporeal circuit
- Dialysate passes on opposite side of membrane
- High efficiency system
- May be poorly tolerated by critically ill patients
- High level of complexity
- No devices specifically for children
- Vascular access/ heparin

Continuous Renal Replacement Therapy (CRRT)



- Continuous hemofiltration technique, often used for critically ill patients
- Technically similar to HD
  - **SLOW:** ICU patients may not tolerate rapid ultrafiltration with HD
  - **CONTINUOUS:** Preserve metabolic stability; maintain fluid balance for oliguric patients who require high daily input (IV medications, parenteral nutrition)

Trends in Pediatric RRT



Warady et al, Pediatr Neph 2000, 15:11-3

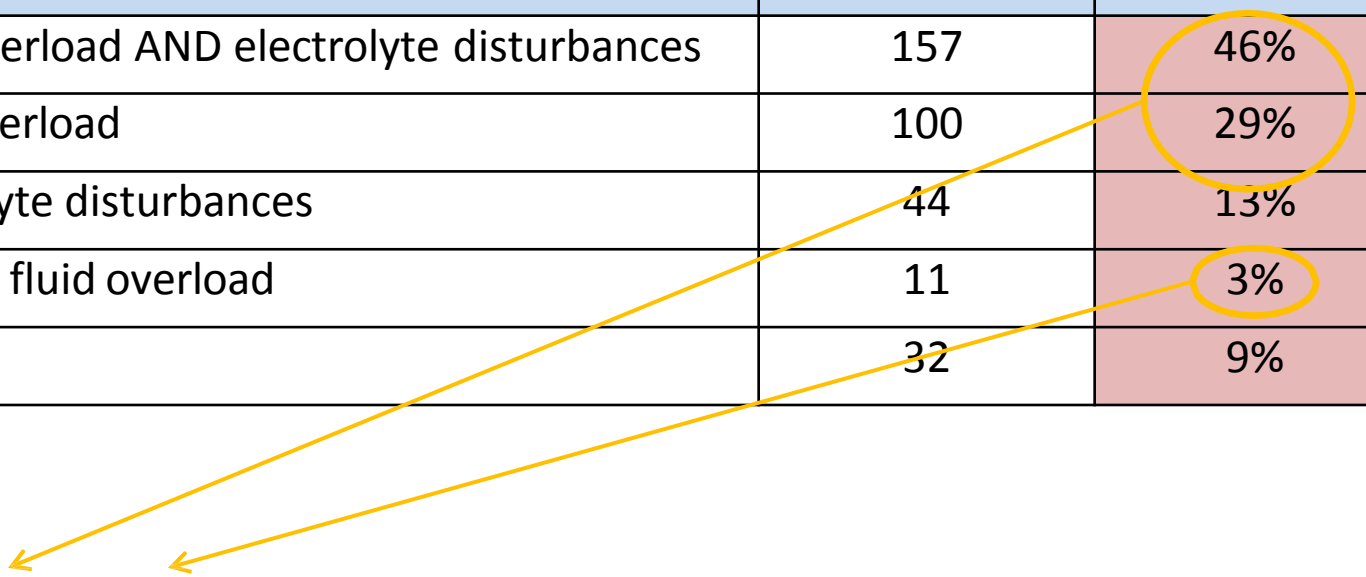
Why CRRT? Indications:

- CRRT typically performed in
  - Critically ill children
  - With oligo-anuric AKI with fluid overload
  - That have failed medical management
- CRRT indications in lieu of HD or PD
  - Hemodynamic instability (accurate, predictable UF over extended time)
  - Large volume needs (nutritional support, FFP, high volume meds)
  - Unusable peritoneal membrane
  - Any condition that makes IHD very difficult

CRRT Indications

ppCRRT Data (n=344)

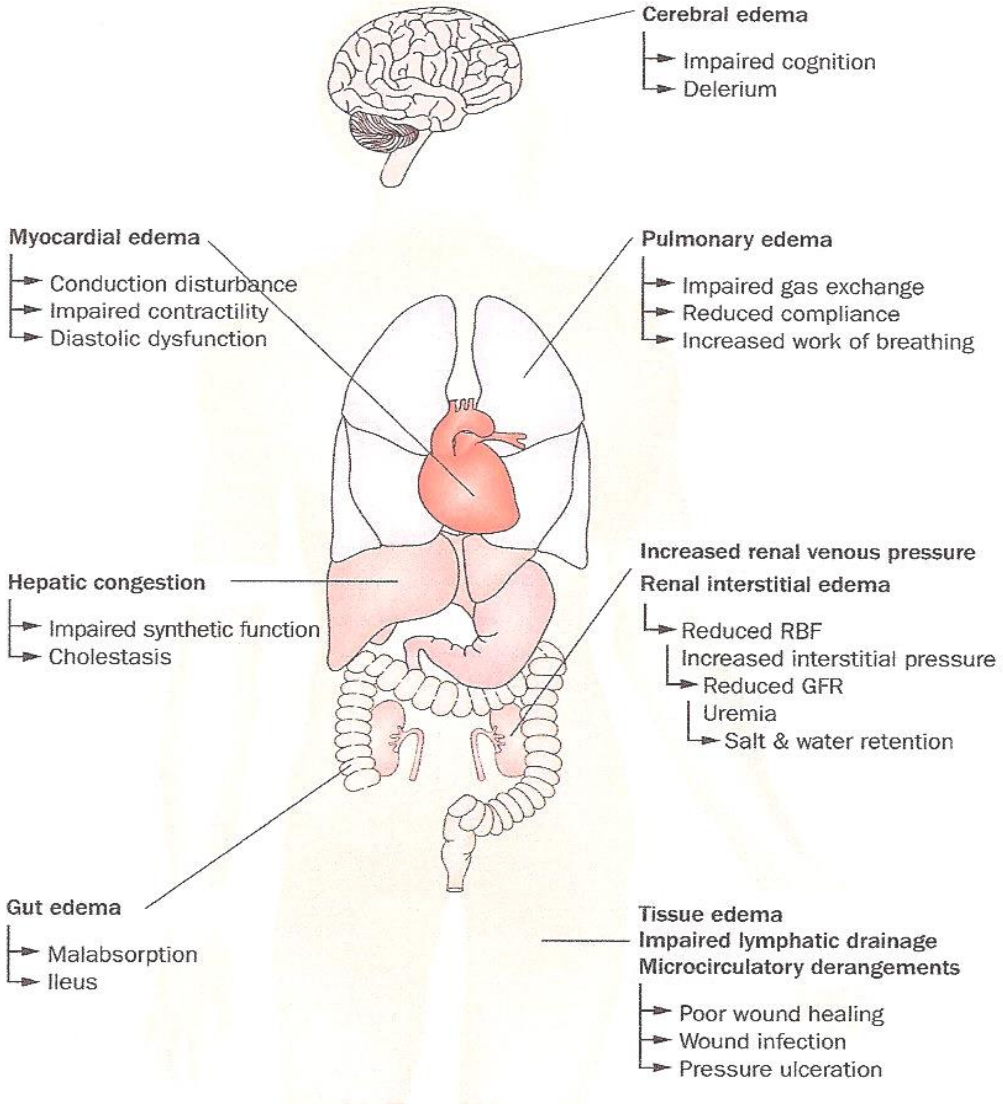
Indication	Patients	% of cohort
Fluid overload AND electrolyte disturbances	157	46%
Fluid overload	100	29%
Electrolyte disturbances	44	13%
Prevent fluid overload	11	3%
Other	32	9%



78% of patients received CRRT, at least in part, to treat fluid overload

Symons JM, et. al. (2007) **Demographic Characteristics of Pediatric CRRT: A Report of the Prospective Pediatric Continuous Renal Replacement Therapy Registry.** Clin J Am Soc Nephrol 2:732-738.

Potential Clinical Consequences of Organ Edema in Critically Ill Patients



Prowle et al, Nature Revs Nephrol 2009

Outcome in Children Receiving Continuous Venovenous Hemofiltration

Stuart L. Goldstein, MD*; Helen Currier, RN, CNN‡; Jeanine M. Graf, MD§; Carmen C. Cosio, MD§;
Eileen D. Brewer, MD*; and Ramesh Sachdeva, MD§

Percent Fluid Overload Calculation

$$\%\ \text{FO at CRRT initiation} = \left[\frac{\text{Fluid In - Fluid Out}}{\text{ICU Admit Weight}} \right] * 100\%$$

Fluid In = Total Input from ICU admit to CRRT initiation
Fluid Out = Total Output from ICU admit to CRRT initiation

Pediatrics 2001;107;1309-1312

FO% in the PICU

Fluid overload is associated with impaired oxygenation and morbidity in critically ill children*

Ayse A. Arikan, MD; Michael Zappitelli, MD, MSc; Stuart L. Goldstein, MD; Amrita Naipaul, NP; Larry S. Jefferson, MD; Laura L. Loftis, MD

FO% occurs early in PICU

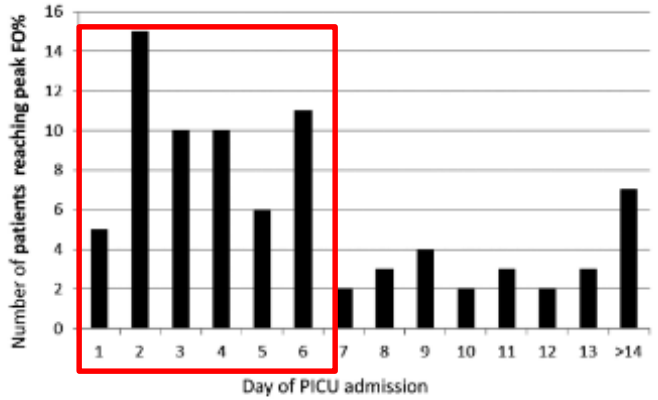


Figure 1. Timeline of occurrence of peak fluid overload percent (*FO%*) during the pediatric intensive care unit (*PICU*) admission. On average, peak FO% was first achieved on day 5.7 ± 4.2, median 4.5, 74% or patients reached peak cumulative fluid overload on day 7 or earlier.

15 – 20% threshold

Table 3. Relationship between total fluid overload percent and oxygenation index

Total Fluid Overload %	Regression Coefficient	*p*
2.5%	0.05	.76
5%	0.05	.92
7.5%	0.05	.56
10%	0.08	.38
12.5%	0.10	.16
15%	0.12	.004
17.5%	0.20	<.001
20%	0.31	<.001

Does reducing FO% with CRRT help?

Impact of Continuous Renal Replacement Therapy on Oxygenation in Children with Acute Lung Injury after Allogeneic Hematopoietic Stem Cell Transplantation

Lama Elbahlawan, MD[1], Nancy K. West, BSN, RN, CCRP[2], Yvonne Avent, MSN, APRN-BC[3], Cheng Cheng, PhD[4], Wei Liu, PhD[4], Raymond C. Barfield, MD, PhD[5], Deborah P. Jones, MD[6], Surender Rajasekaran, MD[7], and R. Ray Morrison, MD[1]

Table III

Median change in respiratory, ventilator, hemodynamic, and laboratory values 24 hours before and 48 hours after CRRT

Measurement	n[1]	Median Change	Range	p[2]
$PaCO_2$ (torr)	29	+0.77	(−37.05 to +83.25)	0.49
PaO_2 (torr)	29	+ 0.97	(−29.83 to +54.00)	0.08
PaO_2/FiO_2	29	+ 43.00	(−88.61 to +264.91)	0.0062
FiO_2	29	−0.05	(−0.33 to +0.28)	0.0495
PIP (cm H_20)	25	−1.50	(−17.50 to +15.50)	0.09
PEEP (cm H_20)	25	0.00	(−8.00 to +7.75)	0.60
Paw (cm H_20)	28	−0.75	(−7.53 to +16.25)	0.50
Fluid balance/wt (mL/kg)	29	−12.47	(−121.96 to +30.14)	<0.0001
Mean BP (mmHg)	29	−4.25	(−26.67 to +81.75)	0.63
Heart Rate	29	−9.00	(−61.75 to +32.50)	0.0126
BUN (mg/dl)	29	−10.33	(−109.25 to +23.25)	0.0001
Creatinine (mg/dl)	29	−0.35	(−1.25 to +14.70)	0.0002
HCO_3 (mmole/l)	29	+ 0.38	(−7.61 to +19.87)	0.27
pH	29	+0.01	(−1.36 to +0.23)	0.70

[1] Number of patients with available data;

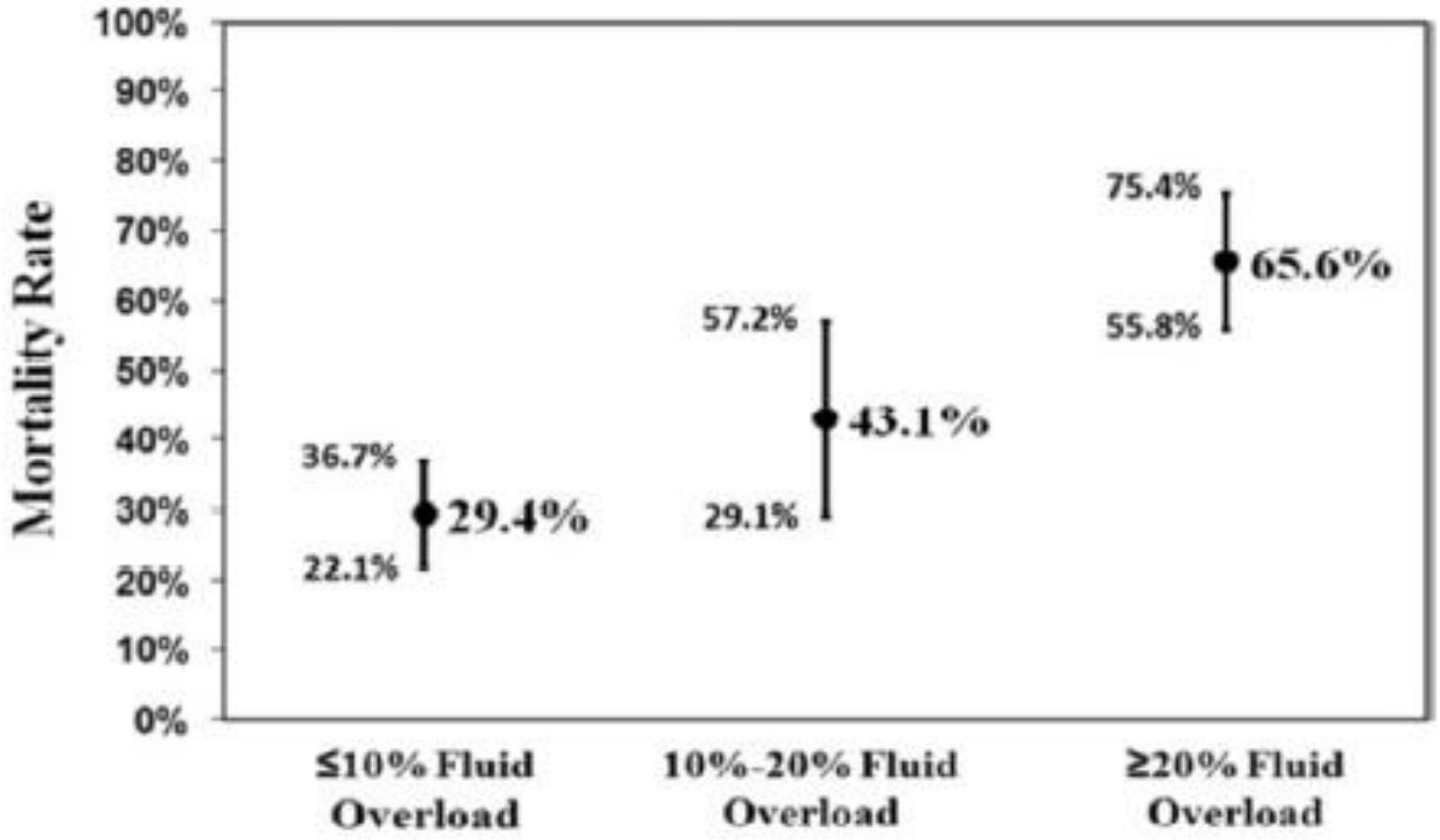
[2] *p* value from signed rank test.

CRRT, continuous renal replacement therapy; pts, patients; $PaCO_2$, carbon dioxide pressure; PaO_2, oxygen pressure; FiO_2, fraction of inspired oxygen PIP, peak inspiratory pressure; PEEP, positive end expiratory pressure; Paw, mean airway pressure; BP, blood pressure; BUN, blood urea

As FO% decreased,

Oxygenation parameters improved

Fluid Overload and Mortality in Children Receiving CRRT: The Prospective Pediatric CRRT Registry



American Journal of Kidney Diseases, Vol 55,No 2 (February), 2010: pp 316-325

When RRT is indicated?

- As soon as fluid overload occurs
- Unless there is excessive solute load
- Reasonable TRESHOLD for initiation of RRT:

fluid overload of 15%

*BUN levels at initiation of RRT was not associated with survival (increased in nonsurvivors)

Bunchman TE.Nature Clinical Practice 2008

Intermittent Therapies - PRO

- (Relatively) Inexpensive
- Flexible timing allows for mobility/transport
- Rapid correction of fluid overload
- Rapid removal of dialyzable drugs
- Rapid correction of acidosis & electrolyte abnormality
- Minimizes anticoagulant exposure

Intermittent Therapies - CON

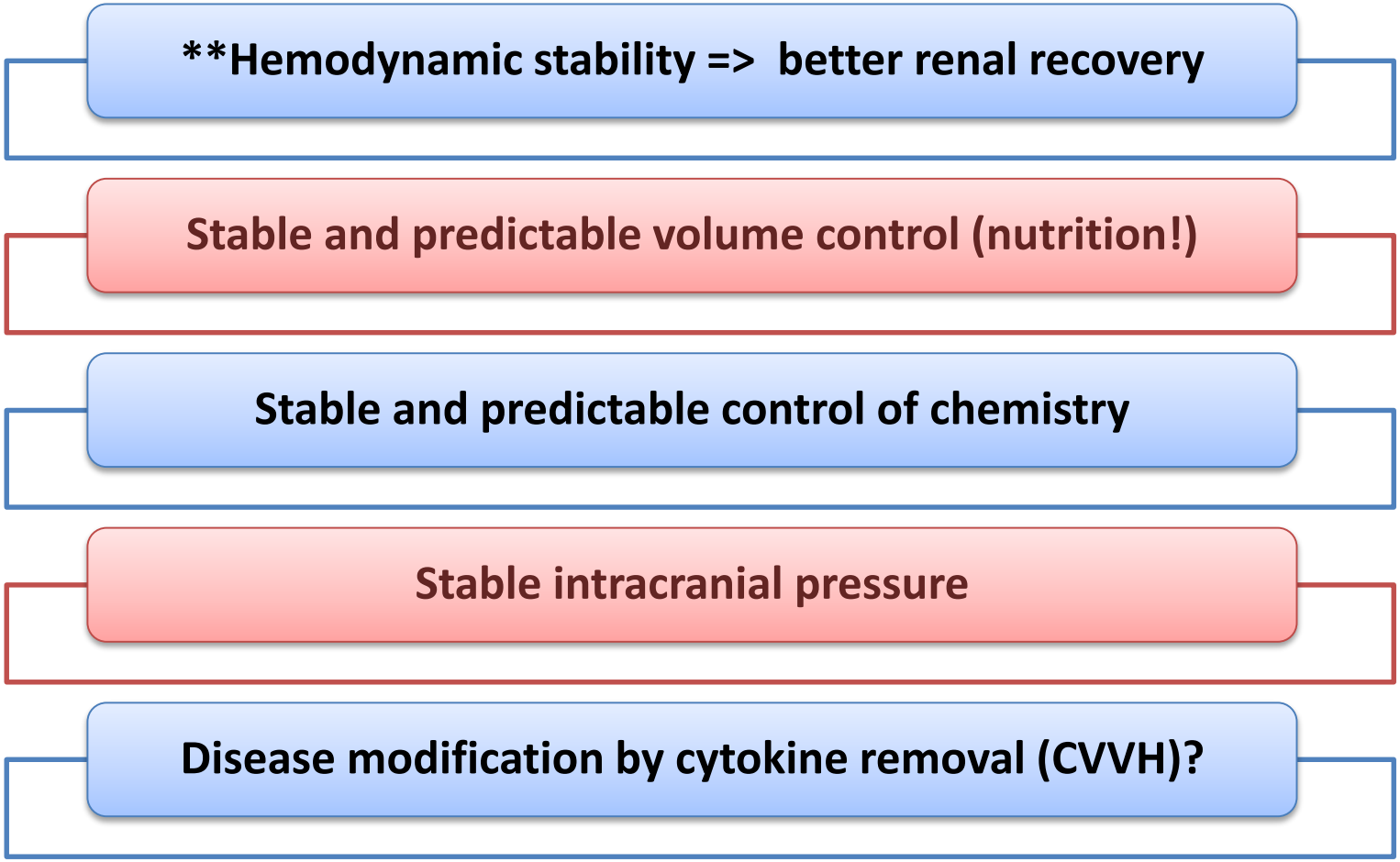
Hypotension 30-60%

Cerebral Edema

Nutritional Provision

- Limited therapy duration
- Renal injury & ischemia
- Gut/coronary ischemia

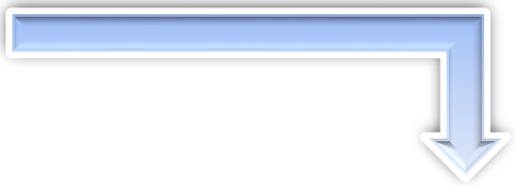
Continuous Therapies - PRO



** Depends on strategy and management

Continuous Therapies - CON

- Anticoagulation requirements
- Higher potential for filter clotting
- Expense – fluids etc.
- Immobility & Transport issues



- Increased bleeding risk
- High heparin exposure

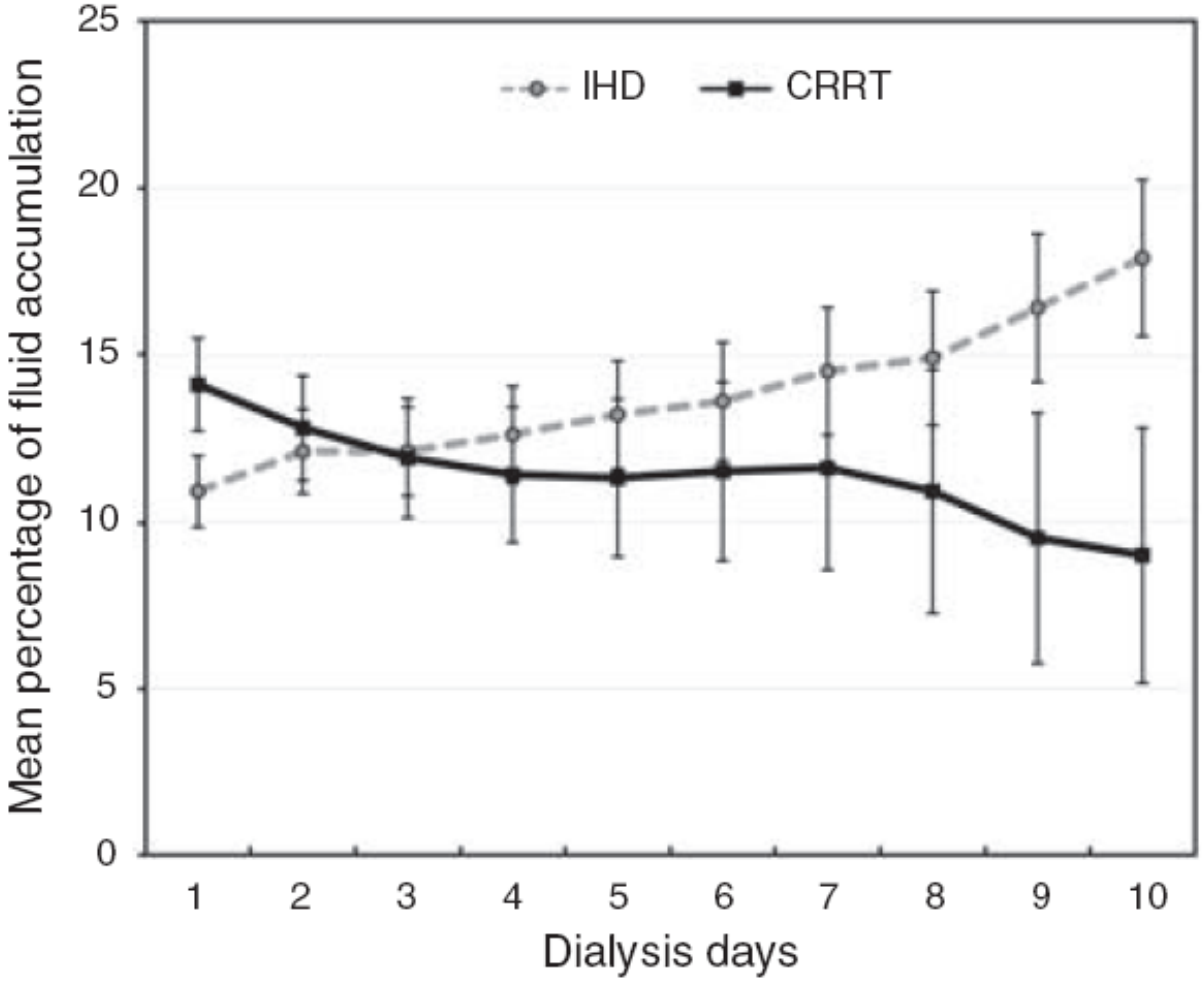
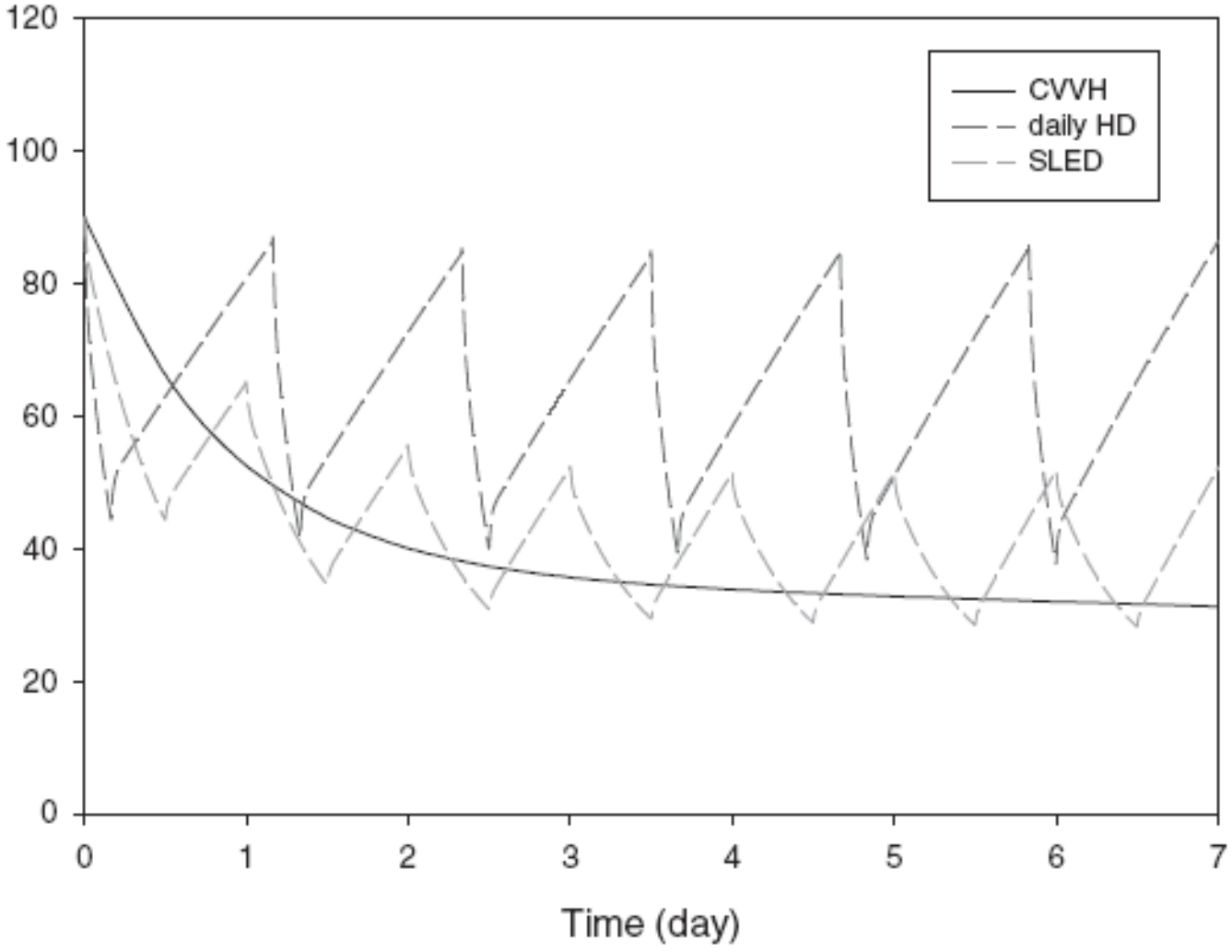


Figure 4 | Fluid accumulation over time in patients on continuous renal replacement therapy and on intermittent hemodialysis.

Bouchard et al, Kidney Int 2009

Uremia Control



Liao, Z *et al*. Artificial Organs 2003; 27: 802-807

Pediatric CRRT Outcomes
General Survival Rates

Study	Age	Pt. #	Survival	Associated with Increased Mortality
Bunchman et. al. (2001)	**6.2y**	**106**	**40%**	**Vasopressor use, non-renal diagnosis**
Goldstein, et. al. (2001)	**8.8y**	**22**	**43%**	**Greater FO**
Gillespie (2004)	**5.1y**	**77**	**50%**	**Greater FO**
Foland et. al. (2004)	**9.6y**	**113**	**61%**	**MODS, Greater FO**
ppCRRT ***-Symons et. al. (2007)*** ***-Sutherland et. al. (2010)***	**8.5y**	**344**	**58%**	**Oncologic disease, MODS, Greater FO,**
Hayes, et. al. (2009)	**5.8y**	**76**	**55%**	**Sepsis, MODS, Greater FO**

Survival rate has improved over time from **40-45%** to **55-60%**

Underlying disease, comorbidities, risk factors determine mortality

Pediatric CRRT Outcomes
Risk Factors for Poorer Outcome

Variable	Odds Ratio (Mortality)	95% Confidence Interval	p-value
Fluid Overload Group			
≥20% FO vs. <10% FO	21.1	5.2 – 85.7	*<0.001*
≥20% FO vs. 10%-20% FO	11.2	1.8 – 68.4	*0.009*
10%-20% FO vs. <10% FO	1.9	0.33 – 10.8	*0.48*
Oncologic Diagnosis	5.8	2.5 – 13.9	<0.001
Diagnosis of MODS	3.7	1.4 – 9.9	0.008
Sepsis Diagnosis	3.6	1.3 – 9.8	0.01
Convective CRRT Modality	0.49	0.28 – 0.86	0.01
PRISM II PICU Admission	1.04	1.0 – 1.1	0.07
IEM/Intoxication Diagnosis	3.4	0.75 – 15.2	0.11
Inotrope Number	1.2	0.9 – 1.6	0.17
CRRT Initiated to treat FO	1.5	0.66 – 3.4	0.34
Age at CRRT Initiation	1.01	0.97 – 1.05	0.63
Sex	0.96	0.55 – 1.7	0.88

Sutherland SM et. al. (2010) Fluid overload and mortality in children receiving continuous renal replacement therapy: the prospective pediatric continuous renal replacement therapy registry. Am J Kidney Dis 55:316-325.

Pediatric CRRT Outcomes
Risk Factors: Fluid Overload

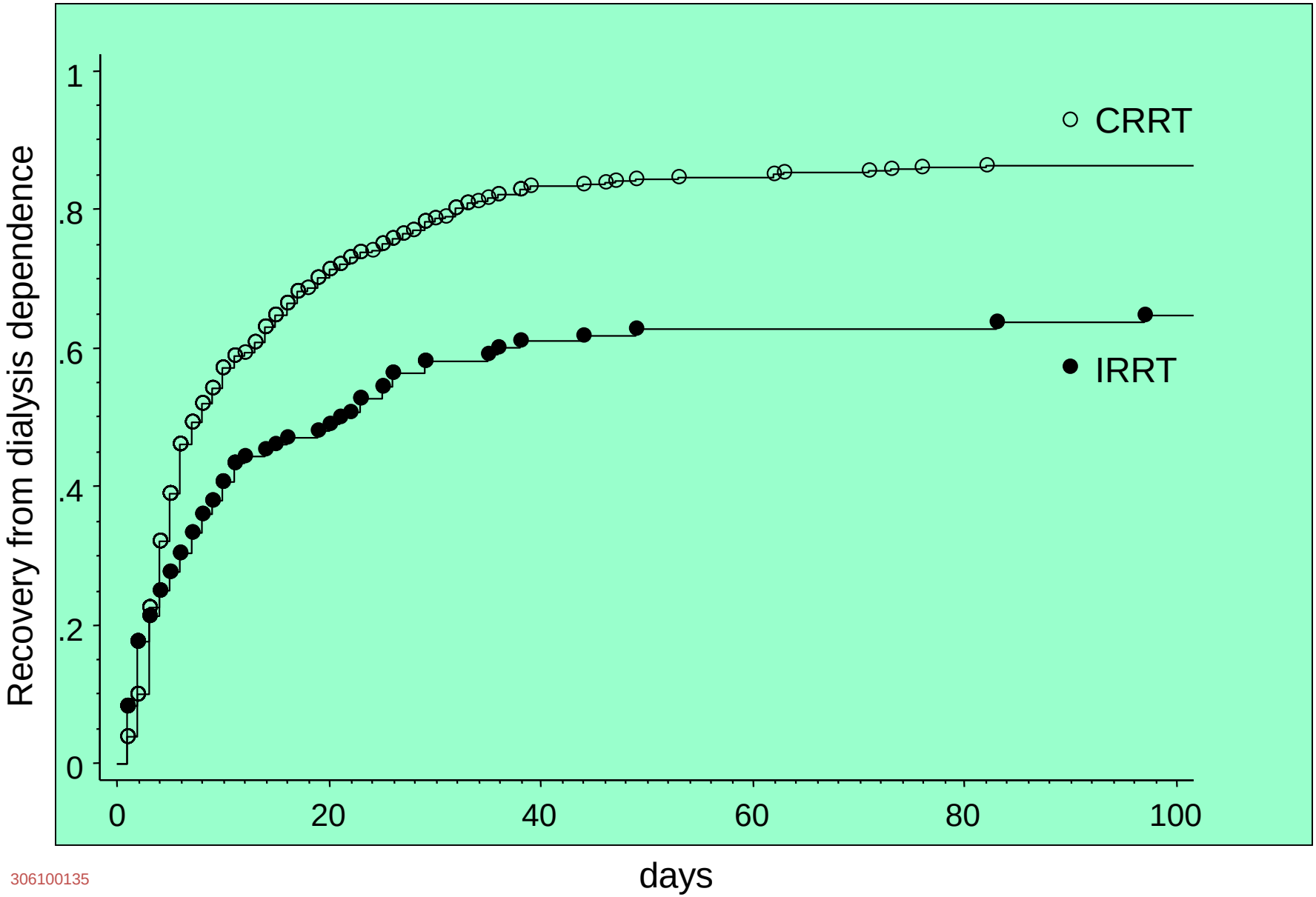
If treated as a continuous variable, odds ratio for FO is 1.03

For every 1% increase in FO, mortality increases by 3%, even after adjusting for severity of illness

Variable	Odds Ratio (Mortality)		
Fluid Overload Group			
≥20% FO vs. <10% FO	21.1		
≥20% FO vs. 10%-20% FO		1.8 – 68.4	*0.009*
10%-20% FO vs. <10% FO		0.33 – 10.8	*0.48*
Oncologic Diagnosis	5.8	2.5 – 13.9	<0.001
Diagnosis of MODS	3.7	1.4 – 9.9	0.008
Sepsis Diagnosis	3.6	1.3 – 9.8	0.01
Convective CRRT Modality	0.49	0.28 – 0.86	0.01
PRISM II PICU Admission	1.04	1.0 – 1.1	0.07
IEM/Intoxication Diagnosis	3.4	0.75 – 15.2	0.11
Inotrope Number	1.2	0.9 – 1.6	0.17
CRRT Initiated to treat FO	1.5	0.66 – 3.4	0.34
Age at CRRT Initiation	1.01	0.97 – 1.05	0.63
Sex	0.96	0.55 – 1.7	0.88

Sutherland SM et. al. (2010) Fluid overload and mortality in children receiving continuous renal replacement therapy: the prospective pediatric continuous renal replacement therapy registry. Am J Kidney Dis 55:316-325.

Recovery from Dialysis Dependence: BEST Kidney Data



306100135

RRT in Critically Ill Children: Summary

- All modalities are available and should be considered depending on the clinical scenario
- CRRT may offer benefits but we lack proof
- CRRT for children requires special considerations given size, equipment
- Acute outcome depends heavily on diagnosis; long-term outcome may include CKD
- Thoughtful planning and teamwork will help us do the best for our young patients

Goal of CRRT:
Simple & quiet procedure...





…satisfied patients

Thoughts to consider…

Pediatric CRRT

Is rarely done but desperately Needed…!





Contact information:

Loai Eid, MD, MSHS, FAAP
Consultant Pediatric Nephrologist
Dubai Hospital - DHA
Mediclinic City Hospital
Email: LaEid@dha.gov.ae
Loaieid@hotmail.com
Mobile: 0562704271

