

# CRRT for the Experience User 1

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AKI & CRRT Conference

February, 2015

## Dose in CRRT: Key concepts

- What dose I should prescribe?
- Prescribed *versus* delivered
- Factors influencing clearance
- It is not only urea...
- Practical Considerations



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## CRRT: treatment goals

- Volume control
- Metabolic control
- Solute clearance
- Safe anticoagulation with minimal clotting



## Case

- 70 year old female with no past relevant medical history; presents with acute cholecystitis and sepsis. After cholecystectomy she develop hospital acquired pneumonia, and Ceftazidime plus Vancomycin was started. She required vassopressors. By the time of nephrology consultation she developed AKI, with oliguria . She weights 70 Kg; she was still on antibiotics, and keterolac was been used as analgesia.
- LABS: Na 138, K 6.5, Cl 109, HCO<sub>3</sub> 16, BUN 60, CrS 4.7, \*GA: pH 7.2 PaCO<sub>2</sub> 40 PaO<sub>2</sub> 90 with FiO<sub>2</sub> 21%, Hb 11 , Hto 30%, WBC 12.500, Plq 104.000.
- She had a positive cumulative fluid balance of 6 liters.



## Chapter 5.8: Dose of renal replacement therapy in AKI

**5.8.1:** The dose of RRT to be delivered should be prescribed before starting each session of RRT. (*Not Graded*) We recommend frequent assessment of the actual delivered dose in order to adjust the prescription. (*1B*)



# Management of Renal Replacement Therapy in Acute Kidney Injury: A Survey of Practitioner Prescribing Practices

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for the VA/NIH Acute Renal Failure Trial Network

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## Survey of 26 questions

7 questions for IHD and SLED that included:

- target dosage of therapy
- whether and how frequently delivered dose was assessed

9 questions for CRRT

- characterized dose mL/h vs. mL/kg/h
- no target dosage or assessment of delivered dose was evaluate.

Only 21% of practitioners assessed delivered dialysis dose (IHD).

< 20% of practitioners reported using weight-based dosing of CRRT.

Absence of a consistent standard for prescription and monitoring of RRT during AKI.

Table 2. Management of IHD<sup>a</sup>

Site	Respondents Using IHD	Treatment Frequency (%)							Median Treatment Duration (hr)	Median BFR (ml/min)	Monitoring of Delivered Dosage (No. of Practitioners)
		2/wk	3/wk	Every Other Day	4/wk	5/wk	6/wk	7/wk			
VA sites											
A	5	—	47.8	—	38.1	14.1	—	—	4.0	400	5/5
B	2	—	15.9	25.5	31.8	26.8	—	—	4.0	350	—
C	3	—	75.7	0.5	23.8	—	—	—	4.0	300	—
D	1	—	75.0	—	13.0	12.0	—	—	3.5	300	—
E	4	—	69.1	—	12.7	18.2	—	—	4.0	310	1/4
F	7	1.9	65.4	0.3	29.9	1.6	0.9	—	4.0	400	1/7
G	3	3.1	60.6	—	24.4	11.9	—	—	4.0	300	—
H	7	—	45.9	5.4	22.5	16.2	6.9	3.0	4.0	300	1/7
I	4	—	40.6	—	29.5	18.9	6.0	5.0	4.0	350	—
J	1	—	69.0	—	15.0	10.0	5.0	1.0	4.0	350	—
K	6	—	13.3	14.8	26.7	29.2	16.1	—	3.25	300	2/6
L	3	—	49.5	7.8	24.5	7.3	5.5	5.4	3.0	350	—
M	4	—	39.4	38.0	16.9	—	—	10.6	3.5	360	—
N	5	—	18.2	18.1	36.8	13.3	6.6	7.1	4.0	300	—
O	3	—	37.5	—	22.5	35.0	38.0	1.2	3.5	325	—
P	5	—	90.0	—	—	—	10.0	—	4.0	350	—
all VA	63	0.7	51.4	5.7	25.7	10.9	3.7	2.0	4.0	350	10/63
Non-VA sites											
Q	— <sup>b</sup>	—	88.9	11.1	—	—	—	—	4.0	350	— <sup>b</sup>
R	4	—	56.9	15.7	13.7	6.7	1.2	5.9	3.0	325	—
S	6	—	73.8	2.9	23.1	18.4	—	—	4.0	350	5/6
T	7	—	23.1	2.5	54.4	15.0	2.5	2.5	3.5	350	—
U	13	—	16.5	11.6	55.2	8.0	0.7	8.0	4.0	350	—
V	5	—	81.5	—	14.8	3.7	—	—	4.0	300	1/5
W	11	—	77.2	1.8	13.5	3.9	2.2	1.4	3.5	375	10/11
all non-VA	46	—	41.8	8.3	36.7	6.8	1.2	5.2	4.0	350	16/46
Combined VA/non-VA sites											
X	7	—	12.9	2.2	17.9	41.2	16.6	9.2	3.5	400	—
Y	12	1.2	57.8	1.8	29.9	4.2	5.1	—	4.0	350	1/12
all combined	19	0.9	45.5	1.9	26.6	14.3	8.2	2.5	4.0	350	1/19
All sites	128	0.4	45.4	6.4	31.6	9.3	3.2	3.8	4.0	350	27/128

<sup>a</sup>BFR, blood flow rate; IHD, intermittent hemodialysis.

<sup>b</sup>Site provided aggregate data for all practitioners.



## Dose of CRRT

- For most small solutes, concentration in ultrafiltrate approximates that of plasma water.
- Since dialysate flow  $\ll$  blood flow, equilibration between plasma and dialysate is nearly complete.
- The concentration of small solutes in the effluent is therefore close to that of plasma water.
- Solute clearance therefore approximates effluent flow rate.





## Chapter 5.8: Dose of renal replacement therapy in AKI

5.8.4: We recommend delivering an effluent volume of 20–25 ml/kg/h for CRRT in AKI (1A). This will usually require a higher prescription of effluent volume. (*Not Graded*)



# Post-dilutional CVVH

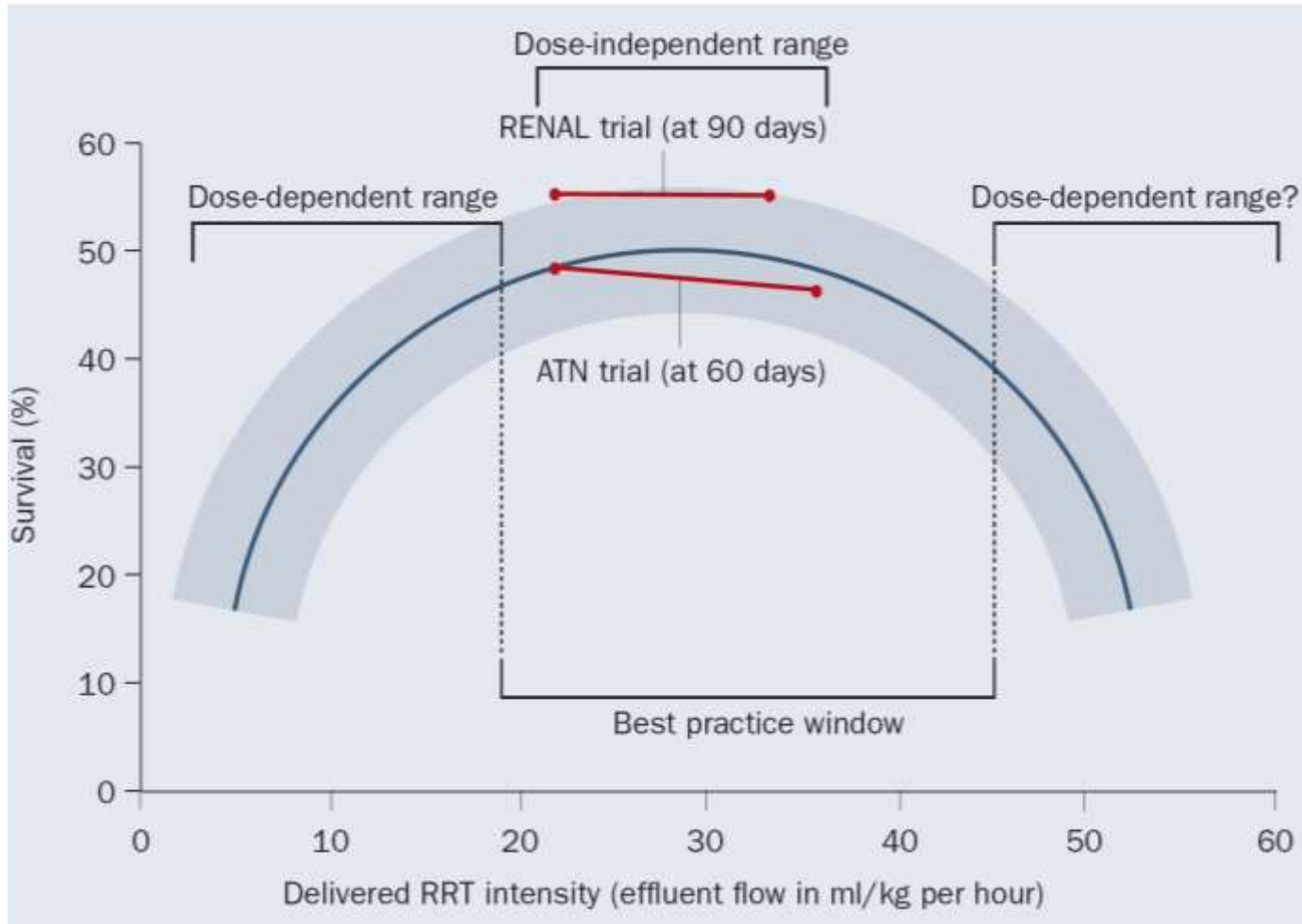
- $K = [\text{effluent flow rate}] Q_e * (C_e/C_b)$
- Post-dilutional CVVH:
  - $Q_b$  100 ml/min.; Hto 30%
  - $Q_{ef}$  1.5 l/h
  - BUN 60 mg/dl
  - FUN 60 mg/dl
- $K_{urea} = 1500 \text{ mL/h} * 60/60$   
= 1500 mL/h  
= **25 ml/min.**  
**(21 mL/kg/hr)**
- Filtration fraction:
  - $Q_{UF}/Q_p$
  - $Q_p = Q_b \text{ ml/hr} * (1-Hto)$
- Filter clotting **FF=25%**
- $FF = 1500 / (6000 * (1-0.30)) = 0.36$  (36%)
- Prevent clotting:
  - *Increase  $Q_b$*
  - *Use pre-dilution*



# Dialysis Dose-Outcome trials and dose measurements

Reference	Assessment of Dose	Delivered Dose		Mortality Intensive vs Control (%)	Difference in Mortality
		Intensive Group	Control Group		
Ronco et al, <sup>12</sup> 2000	Ultrafiltration volume in mL/kg/h	35 and 45 mL/kg/h <sup>a</sup>	20 mL/kg/h <sup>a</sup>	42 and 43 vs 59 <sup>b</sup>	$P < 0.005$
Schiffl et al, <sup>2</sup> 2002	Frequency (3x/wk vs daily)	Weekly delivered Kt/V = 5.8 (mean Kt/V per session = 0.94)	Weekly delivered Kt/V = 3.0 (mean Kt/V per session = 0.92)	28 vs 46	OR, 3.92 (95% CI, 1.68-9.18); $P = 0.01$
Bouman et al, <sup>27</sup> 2002	Ultrafiltration volume in mL/kg/h	48.2 mL/kg/h	19.5 mL/kg/h	37 vs 46 <sup>d</sup>	$P = 0.58$
Saudan et al, <sup>28</sup> 2006	Ultrafiltration volume in mL/kg/h	CVVHDF (24 mL/kg/h replacement fluid + 18 mL/kg/h dialysate)	CVVH (25 mL/kg/h replacement fluid)	46 vs 61 <sup>e</sup>	$P = 0.0005$
Tolwani et al, <sup>29</sup> 2008	Ultrafiltration volume in mL/kg/h	29 mL/kg/h	17 mL/kg/h	64 vs 60 <sup>d</sup>	$P = 0.56$
Palevsky et al, <sup>3</sup> 2008	Ultrafiltration volume in mL/kg/h for CRRT and frequency of session & Kt/V for IHD and SLED	IHD, 5.4 sessions/wk; SLED, 6.2 sessions/wk (session Kt/V = 1.3); CRRT, 35.8 mL/kg/h	IHD, 3 sessions/wk; SLED: 2.9 sessions/wk (session Kt/V = 1.3); CRRT, 22 mL/kg/h	53.6% vs 51.5%	OR, 1.09 (95% CI, 0.86-1.40); $P = 0.47$
Faulhaber-Walter et al, <sup>32</sup> 2009	SUN levels	<90 mg/dL	120-150 mg/dL	70.4% vs 70.7%	$P = 0.97$
Bellomo et al, <sup>30</sup> 2009	Ultrafiltration volume in mL/kg/h	40 mL/kg/h <sup>a</sup>	25 mL/kg/h <sup>a</sup>	44.7% vs 44.7%	$P = 0.99$

# Delivered RRT dose and survival



## Dose in CRRT: Key concepts

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# Prescribed vs. Delivered

Reference	Dialysis Modality	Prescribed	Delivered	% of Delivered Dose
Evanson et al. 1998	IHD	Kt/V 1.25±0.47	Kt/V 1.04±0.49	83.5%
Evanson et al. 1999	IHD	Kt/V 1.11±0.32	spKt/V 0.9±0.33 eKt/V 0.8±0.28 dpKt/V 0.84±0.30	86.4 – 75.5%
Venkataraman et al. 2002	CRRT	24.5±6.7 mL/Kg/h	16.6±5.4 mL/Kg/h	68%
Tolwani et al. 2008	CRRT	Standard 20 mL/Kg/h High 35 mL/Kg/h	17 mL/Kg/h 29 mL/Kg/h	85% 82%
Vesconi 2009 et al.	CRRT	34.3 mL/Kg/h	27.1 mL/Kg/h	79%



# Effluent Volume in Continuous Renal Replacement Therapy Overestimates the Delivered Dose of Dialysis

Rolando Claude-Del Granado,\* Etienne Macedo,\* Glenn M. Chertow,† Sharon Soroko,\* Jonathan Himmelfarb,‡ T. Alp Ikizler,§ Emil P. Paganini,|| and Ravindra L. Mehta\*

Data from 52 critically ill patients, AKI requiring dialysis (Pre-dilution CVVHDF)

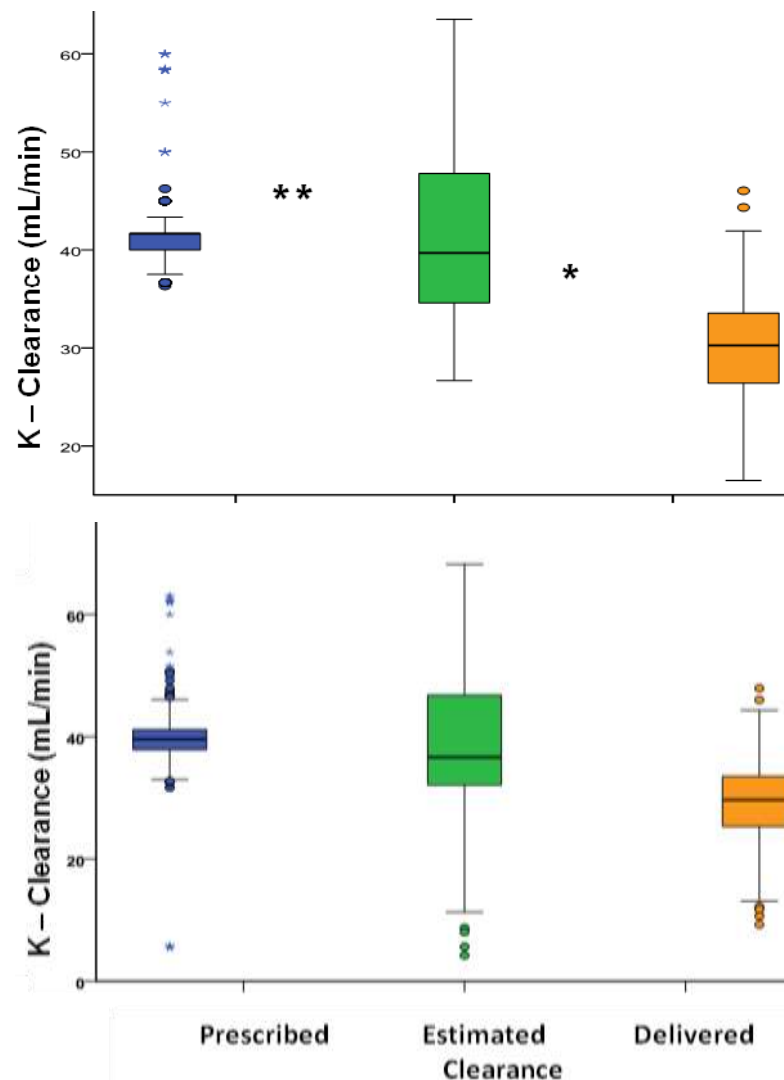
Regional citrate anticoagulation.

Filter efficacy was assessed by calculating FUN/BUN ratios q12 hr.

Prescribed urea clearance (K, ml/min) - Effluent volume rate = Qd (ml/min) + Qr (ml/min) + Qnet (ml/min)

K Estimated = Effluent volume adjusted for effective time of treatment.

K delivered = FUN (mg/dl)/BUN (mg/dl)] x effluent volume rate (ml/min)



# Reasons for Discontinuing CRRT and Filter efficacy

Table 3. Reasons for stopping CRRT

Reasons	Number of Filters	Percentage (%)	FUN/BUN Ratio
Factors affecting treatment time without affecting filter function			
D/C for surgical procedures	10	6.3	0.93 (0.92 to 0.99)
D/C for medical procedures	9	5.7	1.0 (0.95 to 1)
routine filter changes	16	10.1	0.95 (0.84 to 1.0)
machine problems	8	5.0	0.97 (0.85 to 1.0)
transition to IHD	17	10.7	0.96 (0.82 to 0.97)
venous access clot	6	3.8	0.97 (0.96 to 0.98)
physician decision	10	6.3	0.98 (0.94 to 1)
patient or family decision	11	6.9	0.96 (0.94 to 1)
patient recovery	6	3.8	0.95 (0.92 to 0.99)
death	3	1.9	0.98 (0.87 to 1.0)
access change	9	5.7	0.9 (0.87 to 0.95)
Factors affecting filter function			
filter clotted	41	25.8	0.89 (0.83 to 0.94)
filter leak	1	0.63	0.745
low-sieving concentration polarization	12	7.5	0.86 (0.79 to 1.0)





# Delivered CRRT Dose Based on Effluent Collection

*Claire-Del Granado et al, Clin J Am Soc Nephrol 2011*

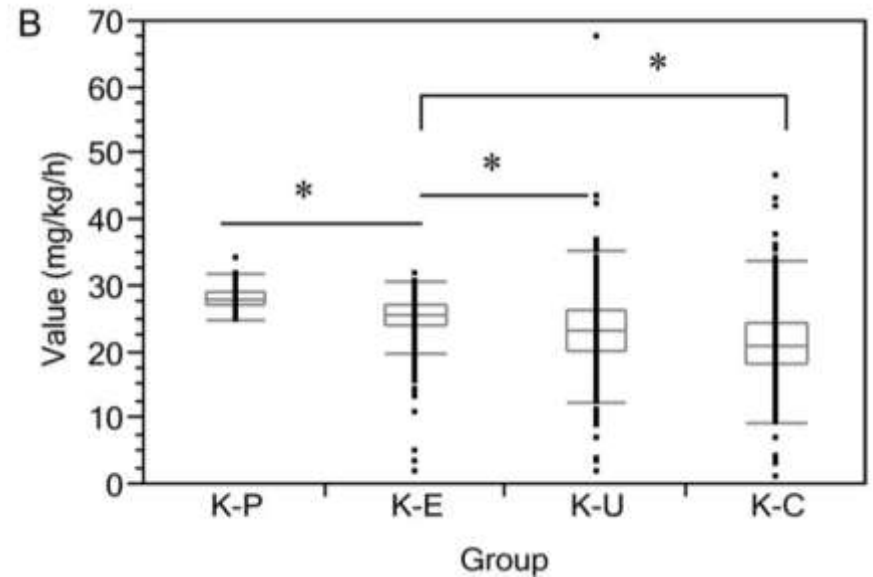
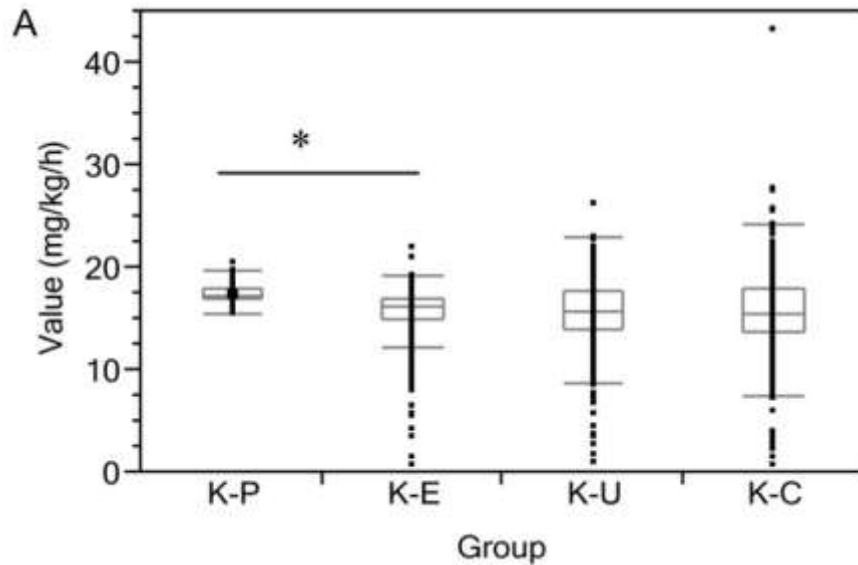
- **Conclusion:**

“Measured effluent volume normalized for effective treatment time significantly overestimates delivered dose of small solutes in CRRT. To achieve a prescribed dialysis dose, effluent-based dose should be increased by 20-25%\* to account for decreases in treatment time and reduced filter efficacy during CRRT.”

Original Article

**Solute clearance in CRRT: prescribed dose versus actual delivered dose**

William D. Lyndon<sup>1</sup>, Keith M. Wille<sup>2</sup> and Ashita J. Tolwani<sup>1</sup>



## Dose in CRRT: Key concepts

- What dose I should prescribe?
- Prescribed *versus* delivered
- **Factors influencing clearance**
- It is not only urea...
- Practical Considerations



# Factors Influencing CRRT Clearances in the ICU

- Patient factors
- Treatment factors



## Treatment Related Factors

- Catheter
- Filter
- Time out of therapy



# Treatment Related Factors

- Catheter
- Filter
- Time out of therapy



## Dialysis

# Complications, Effects on Dialysis Dose, and Survival of Tunneled Femoral Dialysis Catheters in Acute Renal Failure

Kada Klouche, MD, PhD, Laurent Amigues, MD, Sebastien Deleuze, MD, Jean-Jacques Beraud, MD, and Bernard Canaud, MD

Pre-dilution CVVHDF  
Filter 0.9 m<sup>2</sup> AN69  
Anticoagulation LMW Heparin  
Filter change each 72 hrs. or if clotted

Randomized  
-15 patients (46 treatments) PNT catheter  
-15 patients (46 treatments) ST catheter

Prescribed and delivered clearance was assessed

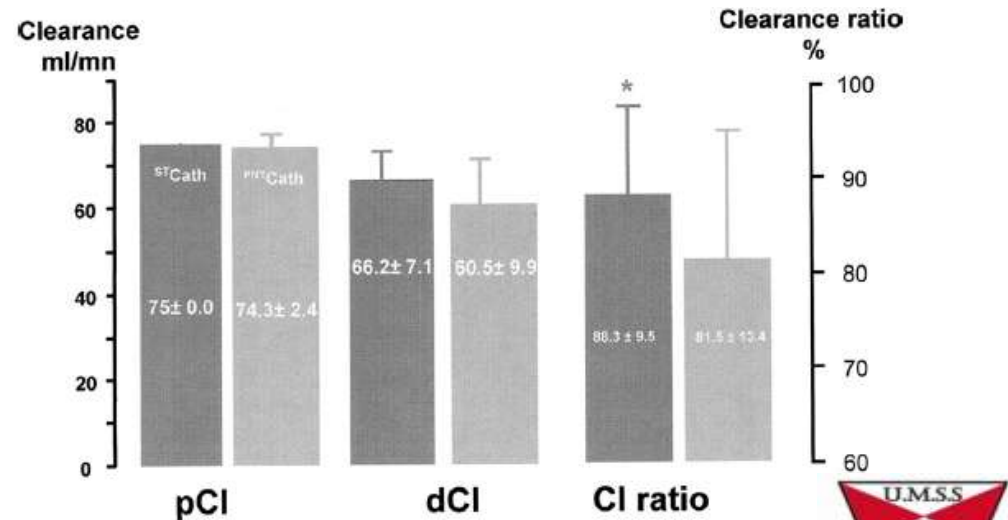
No difference in Q<sub>b</sub>

No difference in recirculation rate

ST catheters less catheter related thrombosis and infection

Table 1. Characteristics of the Population Studied

	Total (N = 30)	<sup>ST</sup> Cath (n = 15)	<sup>PNT</sup> Cath (n = 15)	P
Age (y)	60.7 ± 18.2	61.3 ± 17.6	60.1 ± 19.3	NS
Sex ratio (M/F)	18/30	9/15	9/15	NS
Weight (kg)	77.2 ± 15.6	81.9 ± 12.2	72.4 ± 17.5	NS
APACHE II	29.6 ± 6.6	27.7 ± 5.3	31.5 ± 7.3	NS
LOD score	9.8 ± 2.7	9.7 ± 2.4	9.9 ± 2.9	NS
SAPS II	65.6 ± 16.9	63.3 ± 13.1	67.8 ± 20.3	NS
Septic ARF	23/30	10/15	13/15	NS
Nonseptic ARF	7/30	5/15	2/15	NS
Dialysis time (d)	12.0 ± 8.4	13.5 ± 9.2	10.5 ± 7.4	NS
Duration of catheter use (d)		13.5 ± 9.2	5.6 ± 3.4	0.001



# Treatment Related Factors

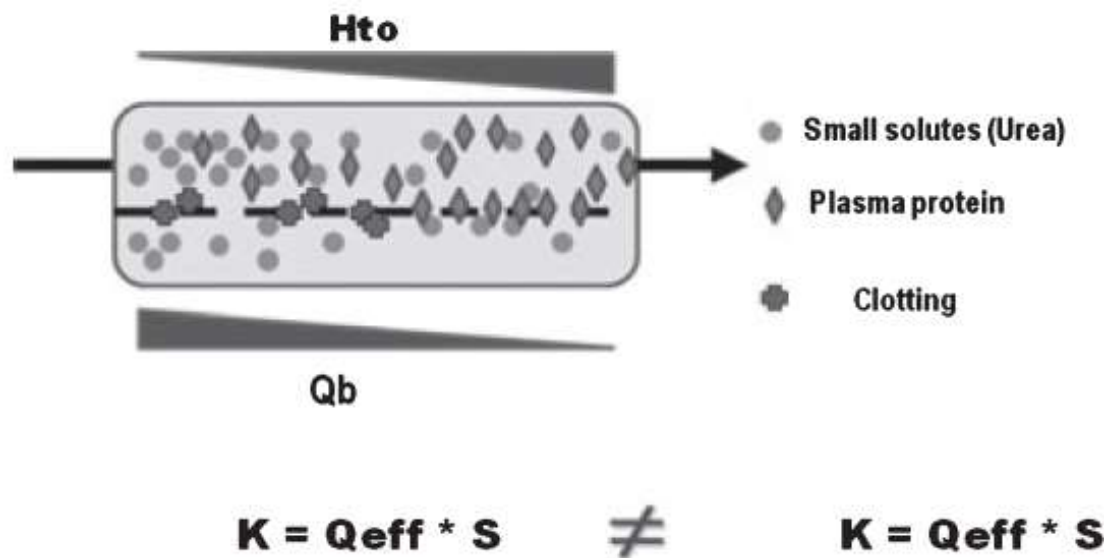
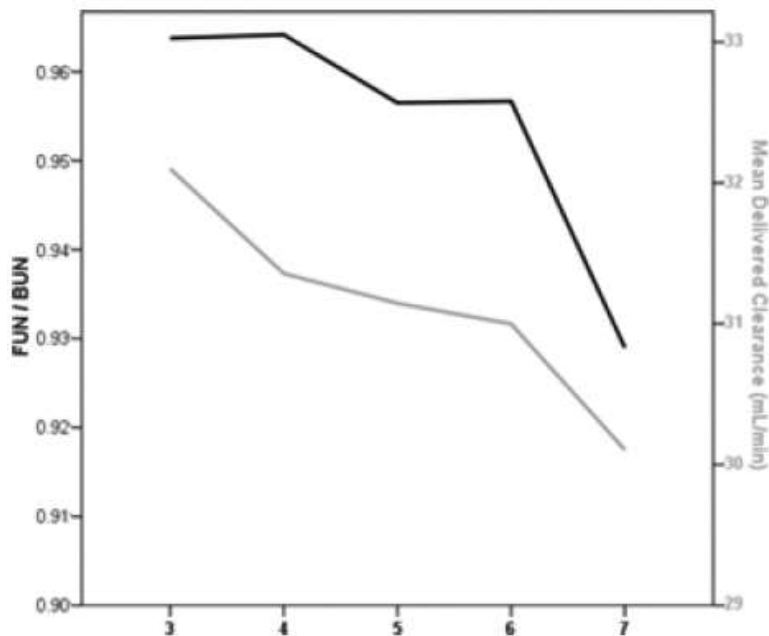
- Catheter
- Filter
  - Down time due to *filter clotting* is the major reason for reduced RRT dose
  - *Concentration polarization* reduces ultrafiltration rate and the filtrate concentrations of various medium / large sized proteins
  - *Convection – Diffusion interactions*
- Time out of therapy





Assessing and Delivering Dialysis Dose in Acute Kidney Injury

Rolando Claire-Del Granado and Ravindra L. Mehta  
 Division of Nephrology and Hypertension, Department of Medicine, University of California San Diego, San Diego, California



Jaffrin MY. Art Organs, 1995.

Claire-Del Granado R and Mehta RL. Sem Dialysis; 2011



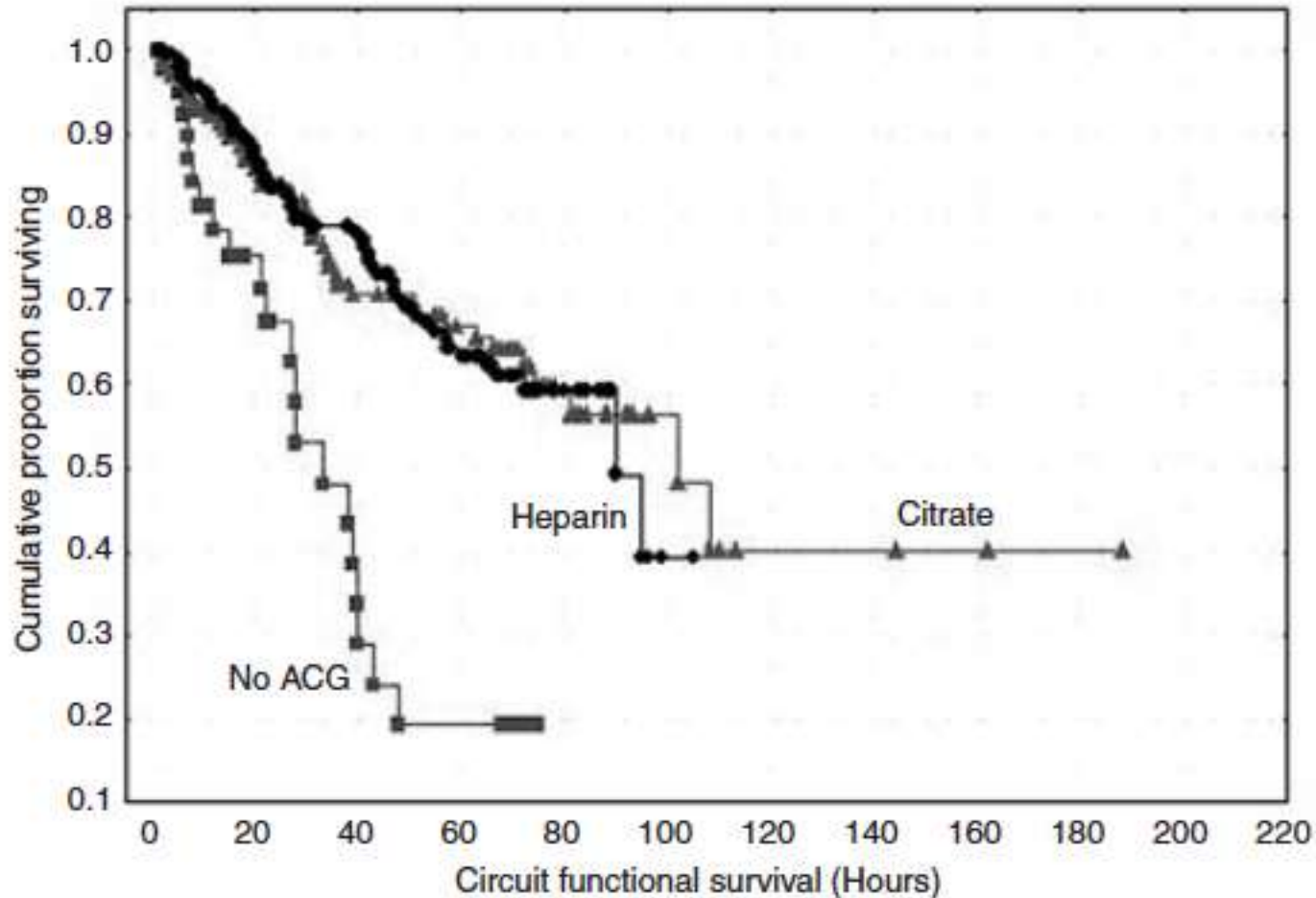
# Post-dilutional CVVH

- $K = [\text{effluent flow rate}] Q_e * (C_e/C_b)$
- Post-dilutional CVVH:
  - $Q_b$  100 ml/min.; Hto 30%
  - $Q_{ef}$  1.5 l/h
  - BUN 60 mg/dl
  - FUN 60 mg/dl
- $K_{urea} = 1500 \text{ mL/h} * 60/60$ 
  - = 1500 mL/h
  - = **25 ml/min.**
  - (21 mL/kg/hr)**
- Filtration fraction:
  - $Q_{UF}/Q_p$
  - $Q_p = Q_b \text{ ml/hr} * (1-Hto)$
- Filter clotting **FF=25%**
- $FF = 1500 / (6000 * (1-0.30)) = 0.36$  (36%)
- Prevent clotting:
  - **Increase  $Q_b$**
  - **Use pre-dilution**
  - **Citrate**



# Multi-centre evaluation of anticoagulation in patients receiving continuous renal replacement therapy (CRRT)

Patrick D. Brophy<sup>1</sup>, Michael J. G. Somers<sup>2</sup>, Michelle A. Baum<sup>2</sup>, Jordan M. Symons<sup>3</sup>, Nancy McAfee<sup>3</sup>, James D. Fortenberry<sup>4</sup>, Kristine Rogers<sup>4</sup>, Joni Barnett<sup>5</sup>, Douglas Blowey<sup>6</sup>, Cheryl Baker<sup>7</sup>, Timothy E. Bunchman<sup>8</sup> and Stuart L. Goldstein<sup>7</sup>



# Citrate Anticoagulation for Continuous Renal Replacement Therapy in the Critically Ill

Heleen M. Oudemans-van Straaten

Department of Intensive Care Medicine, Onze Lieve Vrouwe Gasthuis, Amsterdam, The Netherlands

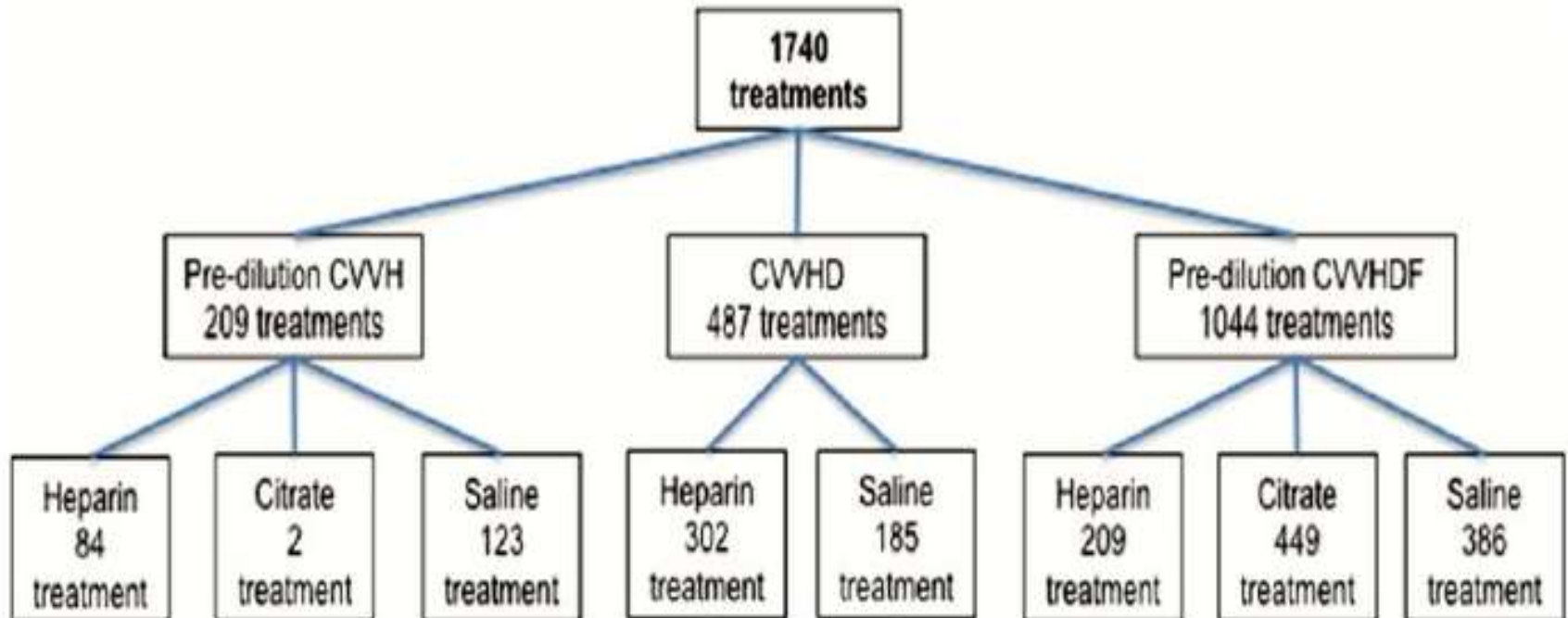
**Table 2.** Main results of the randomized controlled trial comparing citrate to low-molecular-weight heparin anticoagulation for CVVH presented for the per-protocol patients [4]

	Citrate (n = 97)	Nadroparin (n = 103)	p value
Adverse events needing discontinuation of study anticoagulant, %	2	19	<0.001 ←
Bleeding, %	6	16	0.08
Circuit survival time (all reasons), h	27 (13–47)	26 (15–43)	0.68
Renal recovery (all patients), %	69	52	0.02 ←
Renal recovery (surviving patients), %	97	86	0.08
Hospital mortality, %	41 (21–51)	57 (48–62)	0.03 ←
Three-month mortality, %	45 (35–55)	62 (53–72)	0.02 ←



# Anticoagulation, delivered dose and outcomes in CRRT:

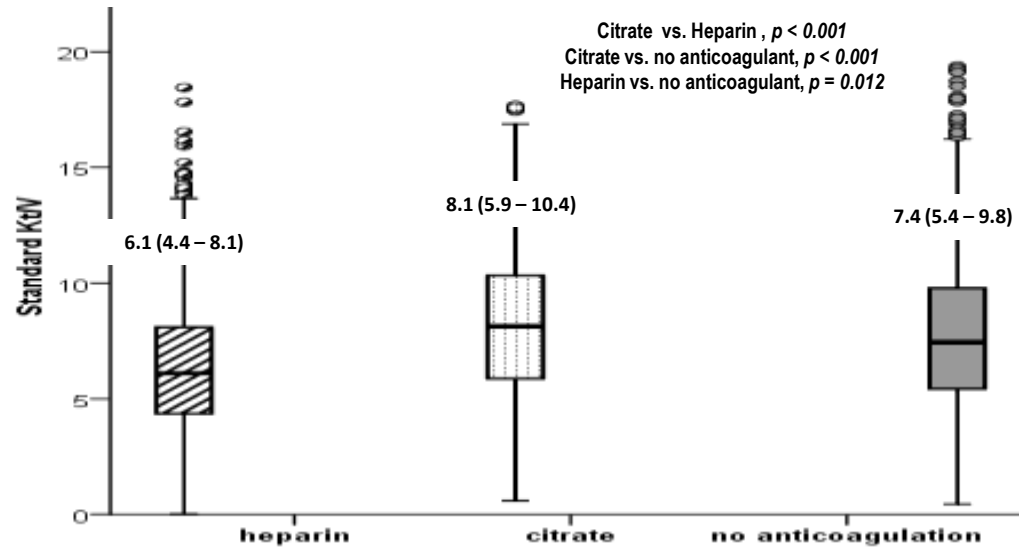
## The program to improve care in acute renal disease (PICARD)



# Anticoagulation, delivered dose and outcomes in CRRT:

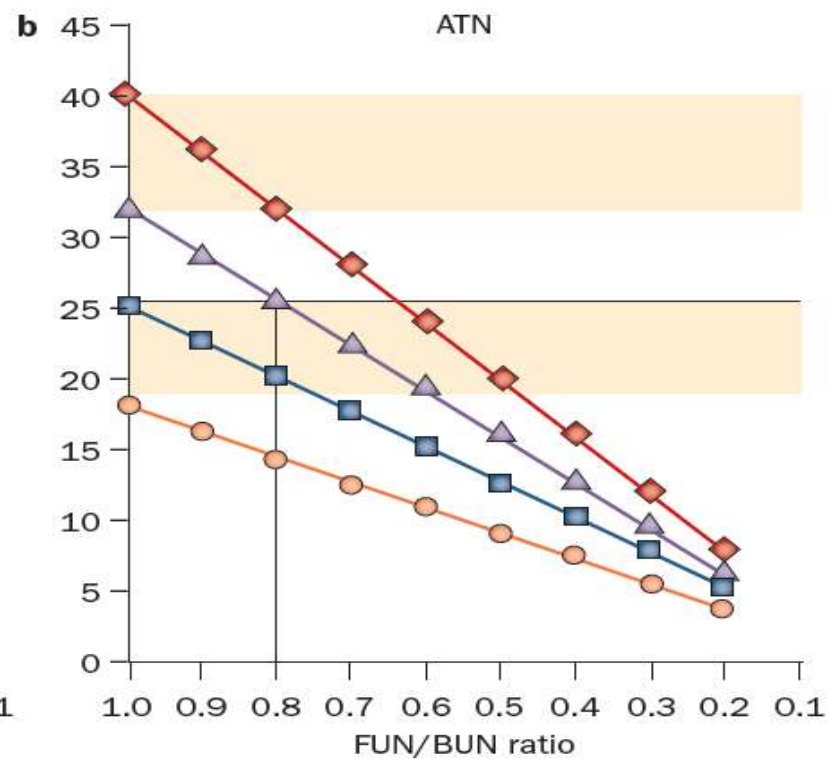
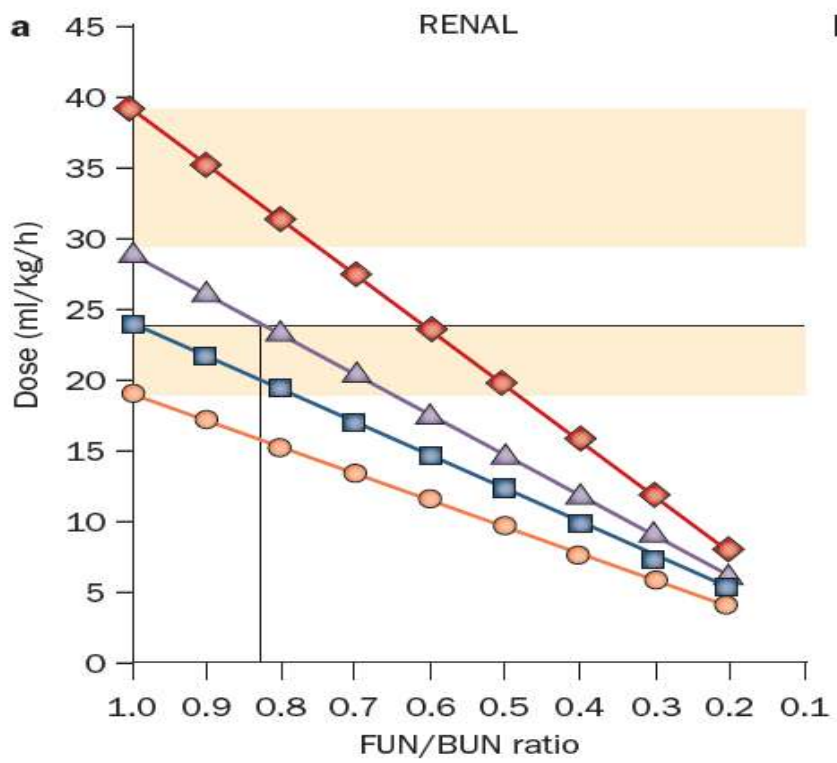
## The program to improve care in acute renal disease (PICARD)

Type of anticoagulant	Median (IQR) Filter Life in Hours
Citrate	48 (20.3-75.0)
Heparin	15.9 (8.5 - 27.0)
No anticoagulant	17.5 (9.5 to 32)
<i>p</i> value	< 0.0001



# Effluent volume and dialysis dose in CRRT: time for reappraisal

Etienne Macedo, Rolando Claure-Del Granado and Ravindra L. Mehta



- 75<sup>th</sup> percentile intensive-dose group
- 25<sup>th</sup> percentile intensive-dose group
- 75<sup>th</sup> percentile low-dose group
- 25<sup>th</sup> percentile low-dose group



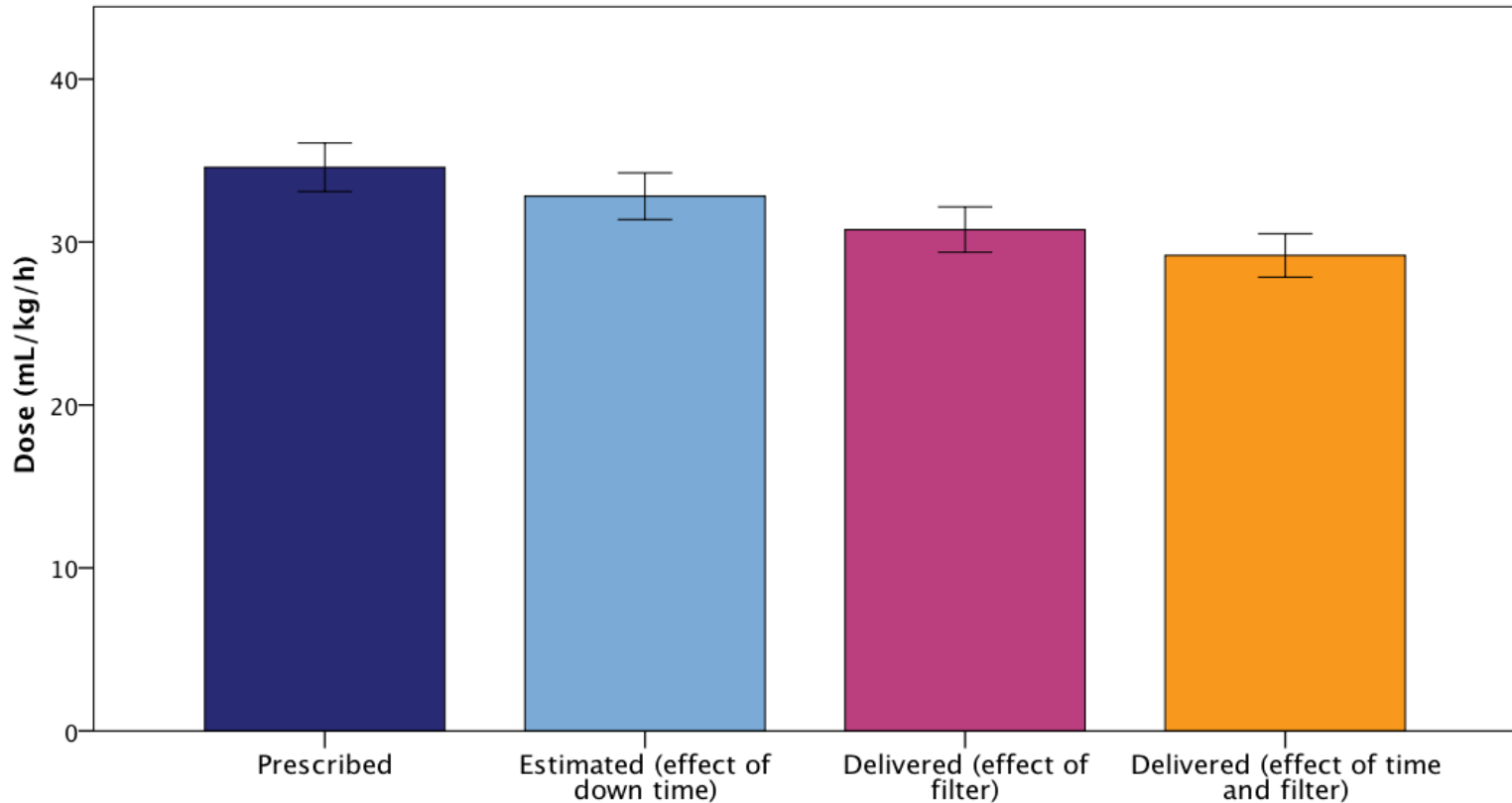
# Treatment Related Factors

- Catheter
- Filter
- Time out of therapy





# The Impact of Down-Time and Filter Efficacy on Delivered Dose of Continuous Renal Replacement Therapy



# Pre-dilution/post-dilution CVVHDF

- $Q_b$  100 mL/min.; Hto 30%
- $Q_{uf}$  1.0 L/hr
- $Q_d$  1.0 L/hr
- $Q_{r\ pre}$  0.5 L/hr
- $Q_{r\ post}$  0.2 L/hr

## Dilution factor:

$$Q_b / (Q_b + Q_r)$$

- Pre-dilution CVVH

$$K = Q_e * (C_e / C_b) * [Q_b / (Q_b + Q_r)]$$

20 mL/min → 17 mL/kg/hr

- Pre-dilution/post-dilution CVVHDF:
  - $Q_b = 200$  ml/min = 12000 mL/hr; Hto 30%
- $K_{urea} = 2500$  ml/hr \* 1 \* [12000 / (12000 + 500)] = 2400 mL/hr  
**= 40 mL/min (34 mL/kg/hr).**
- FF:  
 $1000 / [(12000(1-0.3)) + 500]$   
**0.11**



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# KDIGO Clinical Practical Guideline for Acute Kidney Injury

## Chapter 5.8: Dose of renal replacement therapy in AKI

**5.8.2: Provide RRT to achieve the goals of electrolyte, acid-base, solute, and fluid balance that will meet the patient's needs. (*Not Graded*)**



## Urea clearance as a single parameter to evaluate dose

- A number of studies have suggested a relationship between small-solute control or clearance and patient outcomes during acute IHD.
  - *Smith LH Jr. et al. Post-traumatic renal insufficiency in military casualties. II. Management, use of an artificial kidney, prognosis. Am J Med. 1955 Feb;18(2):187-98.*
  - *Conger JD. A controlled evaluation of prophylactic dialysis in post-traumatic acute renal failure. J Trauma. 1975 Dec;15(12):1056-63.*
- In the 1950s and 1960s, it was conclusively demonstrated during the Korean and Vietnam wars that IHD saved lives



## Urea as the only marker of CRRT dose

- The marker solute (urea) **cannot and does not** represent all the solutes that accumulate in AKI.
- Its **kinetics** and **volume of distribution** are also different from those of the solutes of interest.
- Its removal during CRRT is not representative of the **removal of other solutes.**





# Fluid accumulation, survival and recovery of kidney function in critically ill patients with acute kidney injury

Josée Bouchard<sup>1</sup>, Sharon B. Soroko<sup>1</sup>, Glenn M. Chertow<sup>2</sup>, Jonathan Himmelfarb<sup>3</sup>, T. Alp Ikizler<sup>4</sup>, Emil P. Paganini<sup>5</sup> and Ravindra L. Mehta<sup>1</sup>, Program to Improve Care in Acute Renal Disease (PICARD) Study Group

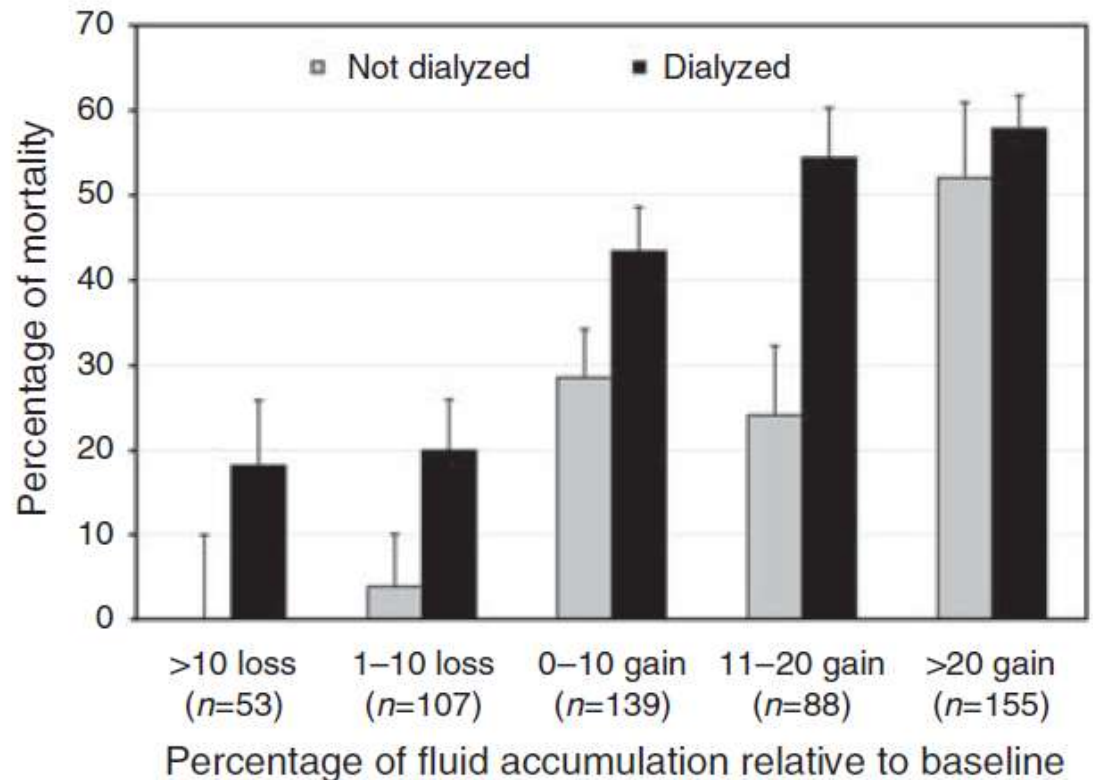
618 patients enrolled in a prospective multicenter observational study (PICARD).

Fluid overload was defined as more than a 10% increase in body weight relative to baseline.

$(\sum \text{daily (fluid intake (L) - total output (L))} / \text{body weight (in kilograms)}) \times 100$ .

Dialyzed patients, survivors had significantly lower fluid accumulation when dialysis was initiated compared to non-survivors after adjustments for dialysis modality and severity score.

Non-dialyzed patients, survivors had significantly less fluid accumulation at the peak of their serum creatinine.



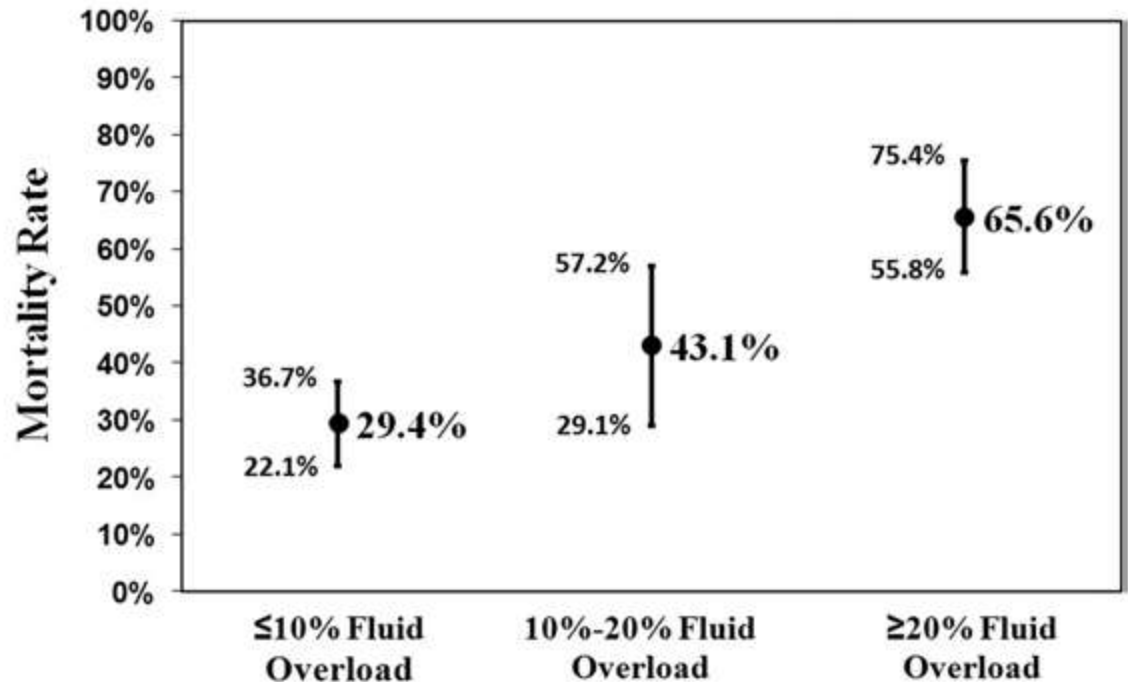


# Fluid Overload and Mortality in Children Receiving Continuous Renal Replacement Therapy: The Prospective Pediatric Continuous Renal Replacement Therapy Registry

Prospective observational study.  
297 children from 13 centers  
across the United States.

Fluid overload from ICU  
admission to CRRT initiation,  
defined as a % equal to (fluid in  
[L] – fluid out [L]) / (ICU admit  
weight [kg]) x 100%.

Patients who developed 20%  
fluid overload at CRRT initiation  
had significantly higher mortality.  
Adjusted mortality OR was 1.03  
(95% CI, 1.01-1.05)



# Proposed parameters for Dose Assessment

**TABLE 2. Proposed parameters for delivered dose assessment**

Parameter	Measurement	Tools
Solute		
Very small waste products	$K^+$ , $Na^+$ , Phosphate $H^-$	Blood levels of K, Na, $PO_4$ Phosphate clearance pH, $HCO_3$ AG, SID <sub>eff</sub> , SID <sub>app</sub> , SIG, Delta gap, Delta ratio.
Small waste products	Urea	Clearance (ml/minutes) EKR (ml/minutes) StdKt/V
Middle-sized molecules	Serum $\beta_2$ Microglobulin	$\beta_2$ Microglobulin clearance
Fluid	Weight (kg) Inputs–Outputs BIA BNP	Weight changes Fluid accumulation Fluid overload BIVA BNP profile



## Dose in CRRT: Key concepts

- What dose I should prescribe?
- Prescribed *versus* delivered
- Factors influencing clearance
- It is not only urea...
- **Practical Considerations**



## Dose in CRRT: Practical considerations

- Clearances should be measured as part of routine care delivery as estimated clearances do not equate delivered.
- Optimizing RRT clearances requires constant assessment and adjustment for operational characteristics and treatment factors.
- Delivered Dose is less than Prescribed and consequently prescribed dose should compensate for the anticipated reduction (approximately 15-25%).
- Solute Clearances are not the sole measure of dialysis adequacy. Fluid removal and fluid balance are equally if not more important parameters to be monitored.

