CRRT ADEQUACY

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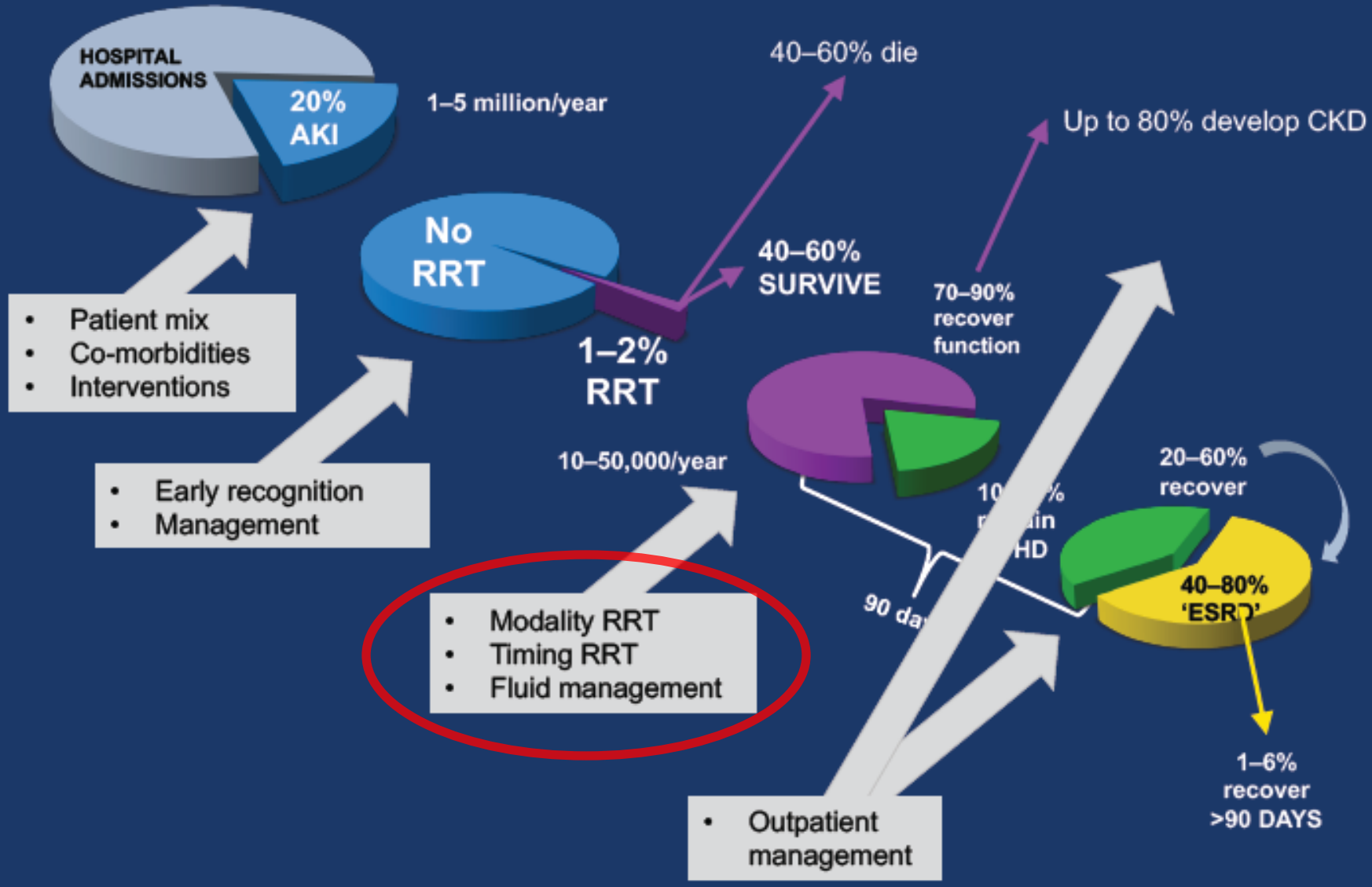
Natural history of AKI-D



HD, haemodialysis

Cerdá J, et al. Clin J Am Soc Nephrol 2015

CRRT treatment goals :

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

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)

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)

Table 4. Management of CRRT[a]

Site	Respondents Using CRRT	CRRT Modalities Used (*n* [%] of Respondents)				Weight-Based Dosing		Non–Weight-Based Dosing	
		AV Modalities	CVVH	CVVHD	CVVHDF	*n* (%)	Median Dosage (ml/kg per h)	*n* (%)	Median Dosage (ml/h)
VA sites									
A	5	—	1 (20.0)	5 (100.0)	—	—	—	5 (100.0)	2000
B	2	—	2 (100.0)	—	—	—	—	2 (100.0)	NR
C	3	—	—	1 (33.3)	3 (100.0)	2 (66.7)	35	1 (3.33)	1850
E	4	—	4 (100.0)	2 (50.0)	2 (50.0)	1 (25.0)	35	3 (75.0)	1000
F	3	2 (66.7)	1 (33.3)	1 (33.3)	1 (33.3)	—	—	3 (100.0)	1000
H	8	1 (12.5)	2 (25.0)	8 (100.0)	—	—	—	8 (100.0)	1000
I	4	—	3 (75.0)	3 (75.0)	4 (100.0)	—	—	4 (100.0)	2500
K	6	—	—	2 (33.3)	4 (66.7)	—	—	6 (100.0)	2000
L	3	—	1 (33.3)	1 (33.3)	2 (66.7)	1 (33.3)	25	2 (66.7)	1800
M	3	—	2 (66.7)	3 (100.0)	3 (100.0)	—	—	3 (100.0)	1100
N	1	—	1 (100.0)	—	—	—	—	1 (100.0)	1500
P	5	—	5 (100.0)	5 (100.0)	4 (80.0)	—	—	4 (100.0)	NR
all VA	47	3 (6.4)	22 (46.8)	31 (66.0)	23 (48.9)	4 (8.5)	35	42 (89.4)	1800
Non-VA sites									
Q	—[b]	—[b]	—[b]	—[b]	—[b]	—	—	—[b]	2000
R	4	—	—	4 (100)	—	—	—	4 (100.0)	1500
S	5	—	4 (80)	1 (20)	—	—	—	5 (100.0)	1600
T	7	2 (28.6)	7 (100.0)	2 (28.6)	7 (100.0)	5 (71.4)	35	2 (28.6)	1000
U	13	—	—	13 (100.0)	13 (100.0)	—	—	13 (100.0)	2400
V	5	—	—	3 (60.0)	3 (60.0)	—	—	5 (100.0)	1000
W	11	2 (18.2)	2 (18.2)	9 (81.8)	4 (36.4)	1 (9.1)	35	10 (90.9)	1500
all non-VA	45	4 (8.9)	13 (28.9)	32 (71.1)	27 (60.0)	6 (13.3)	35	39 (86.7)	1600
Combined VA/non-VA sites									
X	8	2 (25.0)	3 (37.5)	4 (50.0)	6 (75.0)	5 (62.5)	35	3 (37.5)	2250
Y	12	—	5 (41.7)	11 (91.7)	11 (91.7)	5 (41.7)			2300
All sites	112	9 (8.0)	43 (38.4)	78 (69.6)	67 (59.8)	20 (17.9)	35 (IQR 35 to 35)	91 (81.2)	1825 (IQR 1200 to 2400)

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 prescr tion of effluent volume. (Not Graded)

regardless the chosen modality or proportion of replacement fluid given pre or post filter

Use of Clearance to Quantify Dose in RRT

❖ Overview of Clearance :

- Clearance (mL/min) : mass removal rate / blood concentration
- **A steady state is assumed** : net solute generation is balanced by net removal
- Clearance concept → ESRD patients occurred nearly 40 years ago as a way to quantify delivered HD dose, with urea used as a surrogate molecule generally representative of uremic toxicity
- Various urea kinetic modeling → all based on the assumptions of a quasi-steady state for the patient and the validity of a single measurement being representative of dialysis delivery over an extended period of time ; **urea Kt/V**
- Urea kinetic modeling → delivered dose for PD pts

❖ What Clearance?

▪ Surrogate Molecule Considerations :

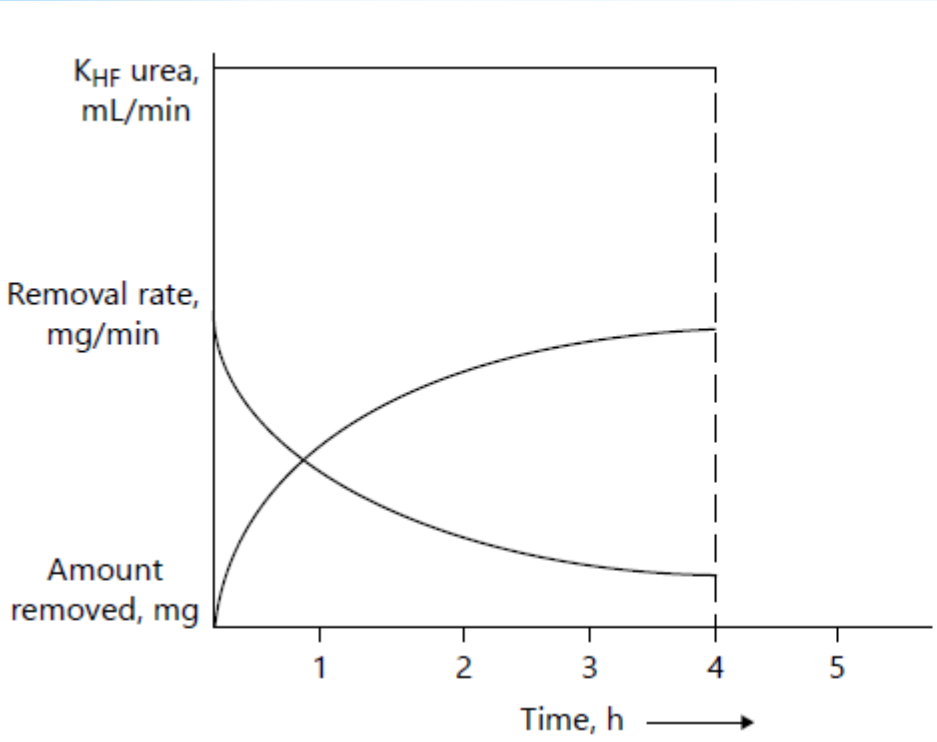
- **Exclusive use of urea** for kinetic modeling and dosing
- kinetics of urea removal is relatively well understood for different dialysis modalities and the molecule **is easily measured** in clinical practice
- While its **actual toxicity** is a matter of debate
- A good surrogate for the "**small solute**" uremic class, which consists classically of highly water-soluble, nitrogenous waste products

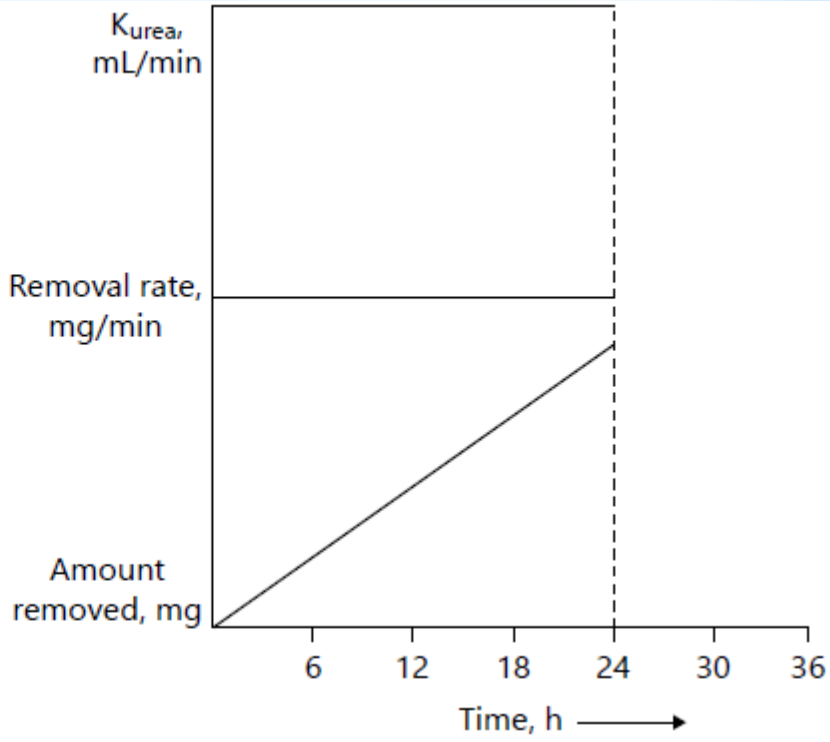
❖Instantaneous vs. Treatment Clearance :

- **Instantaneous clearance** → **gold standard** for the technical assessment of a filter
- **Treatment (time-averaged) clearance** is more commonly used in clinical practice to characterize the overall therapy efficacy for both HD and PD.
- **Kt/v = -Ln (R – 0.008·t) + (4 – 3.5·R) (UF/W)**
- Since this equation was developed for and **validated in maintenance HD patients**, its relevance to critically ill AKI patients can be questioned, since intradialytic urea generation and ultrafiltrate volumes may be substantially different in this latter population
- **Conventional HD and other high-efficiency therapies** → solute kinetics in body compartments outside the vascular space ; not necessarily to **lower efficiency therapies**, such as PD and CRRT, in which a significant difference in inter-compartment and extracorporeal solute transfer rates does not exist.
- Relatively low efficiency of CRRT → unhelpful blood-side instantaneous clearance determinations ; blood passage through the filter does not produce substantial differences between the incoming and outgoing blood concentrations
- Thus, when an instantaneous clearance is determined for a CRRT filter, effluent measurements (product of the flow rate and solute concentration) are used

Relationship between Solute and Mass Removal Rate for Different Modalities

- The relationship between solute removal and clearance is therapy-specific





Dose-response relationship in continuous renal replacement therapy

study	No	Intervention	Population	Risk of Death	ARF duration	Renal Recovery
Ronco 2000	425	20 vs 35 vs 45 ml/kg/h	75% post surgical 12% septic	59% vs 43% vs 42 %(P<0.002)		No Effect
Bouman 2002	106	24-36 vs 72 L/day (20 vs 48 ml/kg/h)	58% post CV surgery , 100% resp failire,100% inotrope	No Effect	No Effect	No Effect
Saudan 2006	206	CVVHF 25 ml/kg/h CVVHDF42ml/kg/h	60 % septic	61% vs 41% (P=0.03)		No Effect
Tolwani 2008	200	20 vs 35 ml/kg/h	54 % septic , 77.5% resp failure	No Effect		No Effect
ATN 2008	1124	20 vs 35 ml/kg/h AND 3/w vs 6/w IHD	63% septic , 80.6% resp failure	No Effect	No Effect	No Effect
RENAL 2009	1508	25 vs 40 ml/kg/h	49.4 % septic , 73.9% resp failure	No Effect	No Effect	No Effect
Joannes Boyau 2013	140	35 vs 70 ml/kg/h	100% septic , 93.7% resp failure	No Effect	No Effect	No Effect

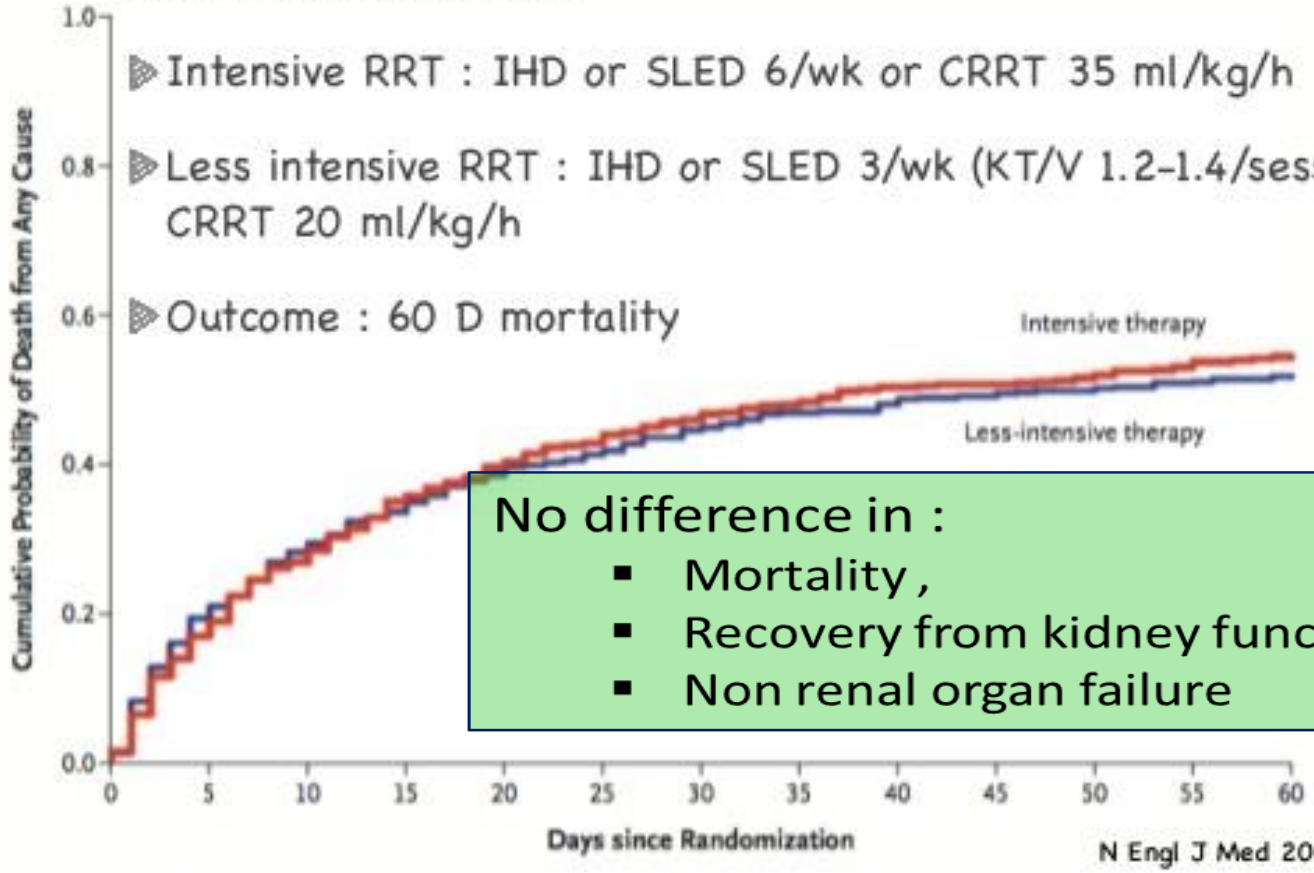
The ATN study

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

The VA/NIH Acute Renal Failure Trial Network*

A

- RCT 1124 AKI in ICU
- Intensive RRT : IHD or SLED 6/wk or CRRT 35 ml/kg/h
- Less intensive RRT : IHD or SLED 3/wk (KT/V 1.2–1.4/session) or CRRT 20 ml/kg/h
- Outcome : 60 D mortality



No difference in :

- Mortality ,
- Recovery from kidney function
- Non renal organ failure

N Engl J Med 2008;359:7-20.

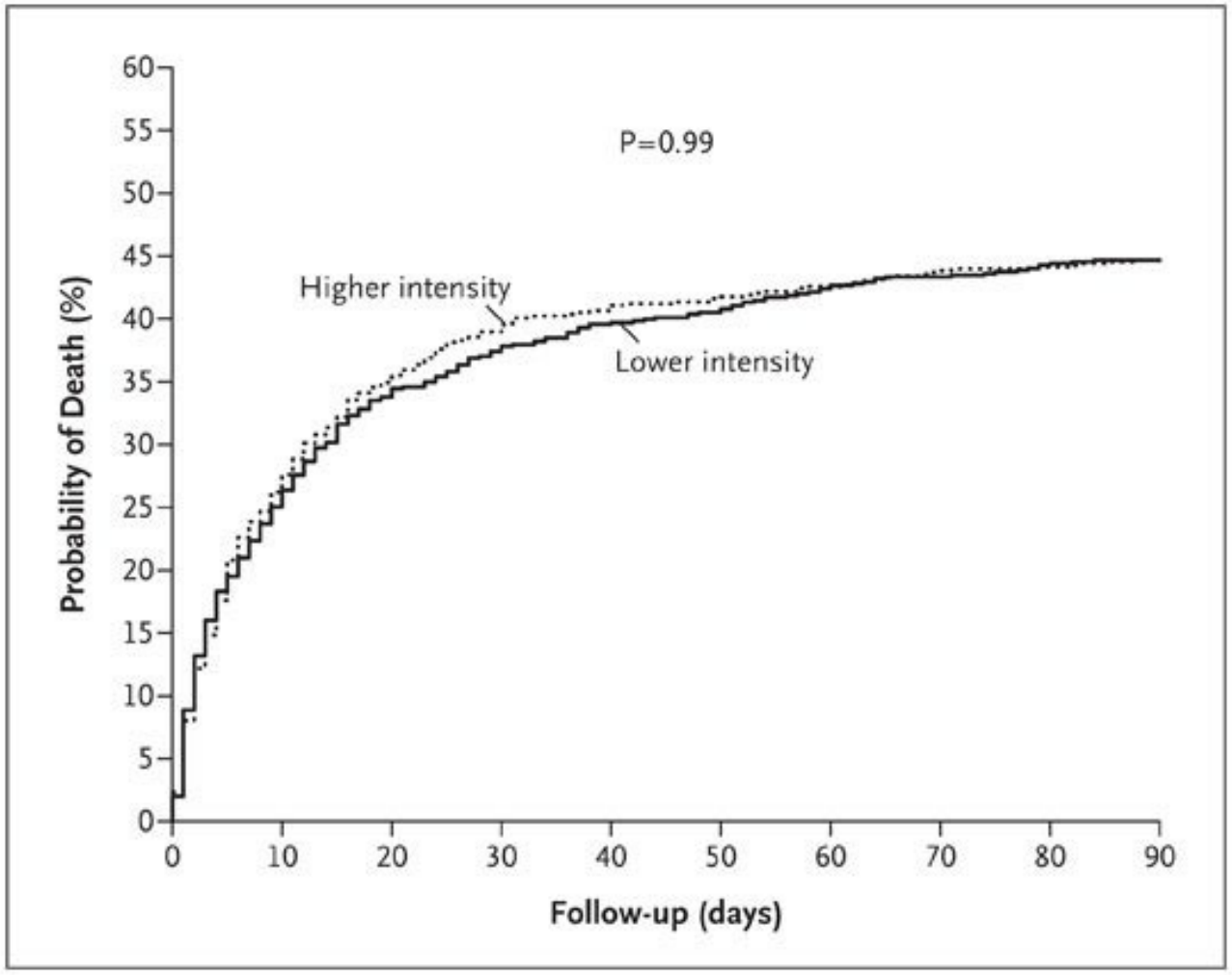
The RENAL study

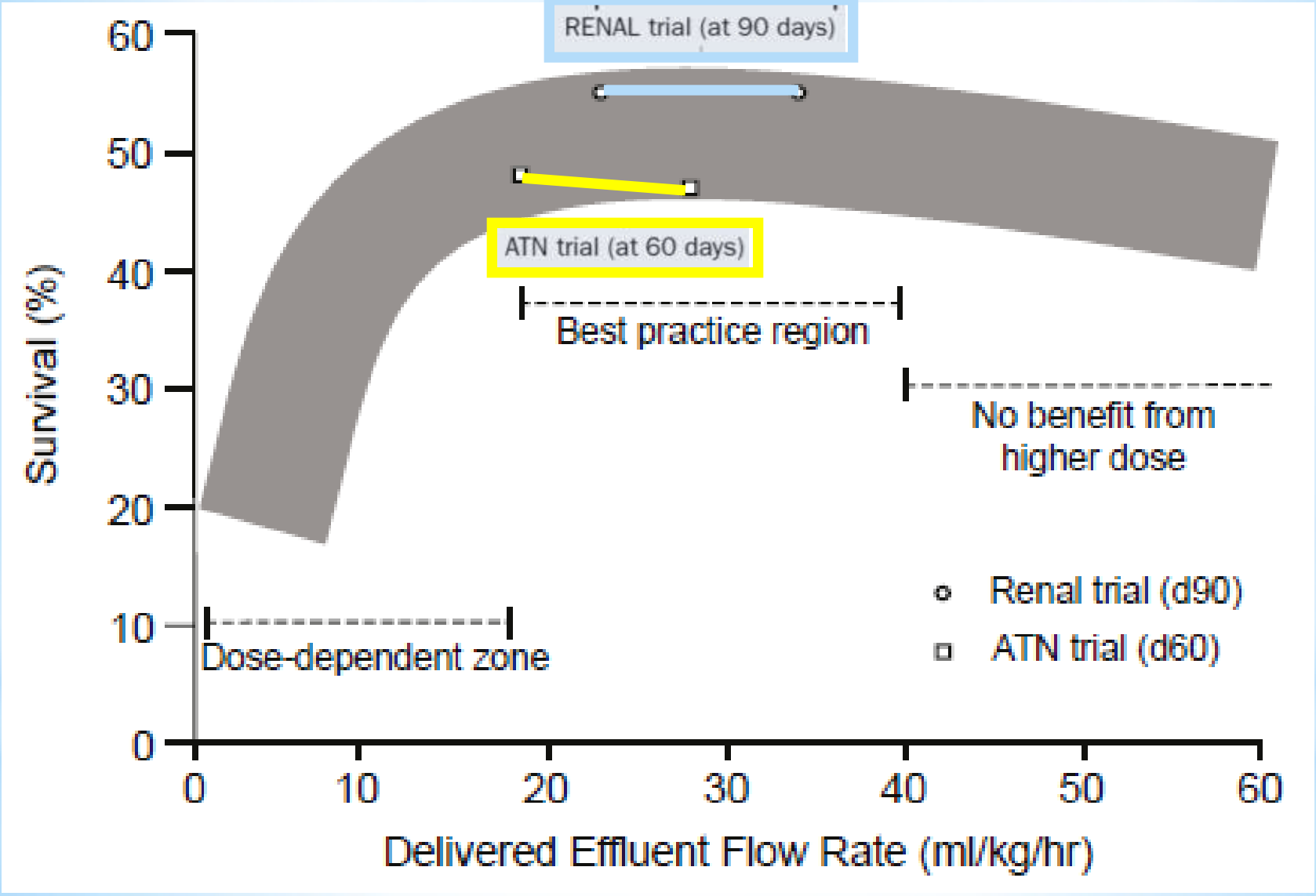
40 mg/kg/h

25 mg/kg/h

Table 3. Primary and Secondary Outcomes.*

Outcome	Higher-Intensity CRRT	Lower-Intensity CRRT	Odds Ratio	P Value†
Death — no./tota				
By day 90			23)	0.99
By day 28			32)	0.52
Place of death —				
ICU			l.273)	0.81
Hospital ward			l.288)	0.60
Outside hosp			).279)	0.63
RRT dependence				
At day 28			79)	0.31
At day 90			92)	0.14
No. of days of RR				0.14
No. of days in ICU				0.95
No. of days in hos				0.79
No. of days of me				0.79
No. of nonrenal o				
0				0.57
1				0.93
2				0.65
3				0.85
4				0.33



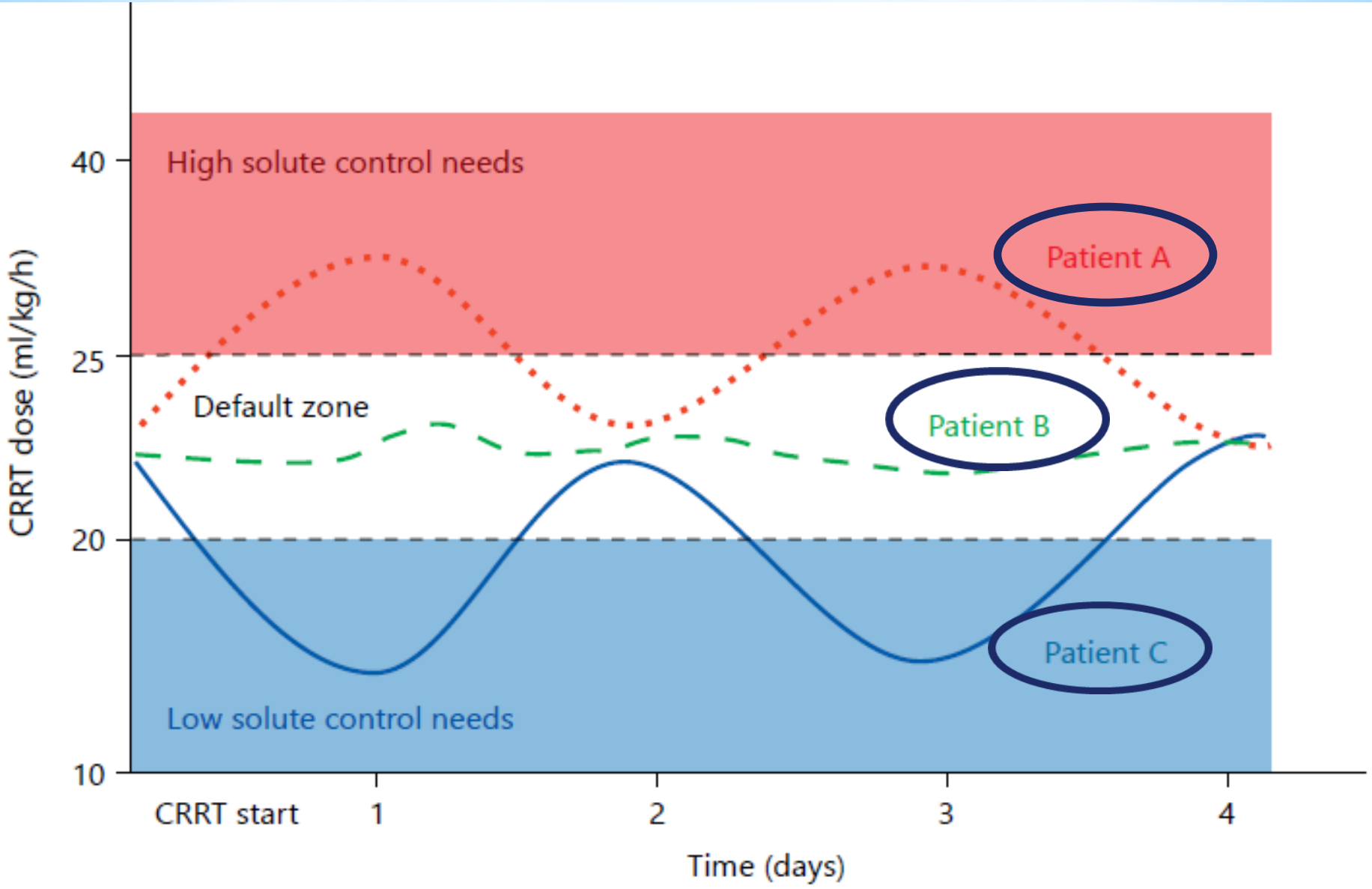

RENAL trial (at 90 days)
ATN trial (at 60 days)
Best practice region
No benefit from higher dose
Dose-dependent zone
Renal trial (d90)
ATN trial (d60)
Survival (%)
Delivered Effluent Flow Rate (ml/kg/hr)
0
10
20
30
40
50
60

Prescribed vs. Delivered dose

Reference	Dialysis Modality	Prescribed	Delivered	% of Prescribed 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±60.33 eKt/V 0.8±40.28 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%

❖ 17th ADQI International Consensus Conference :

- ❑ What is the ideal method to prescribe and measure delivered CRRT dose for solute control?
  - ✓ Default prescribed CRRT : 20–25 ml/ kg/h
  - ✓ Prescribed dose is dynamic. This default prescribed dose can be modified according to patient demand and in response to iterative evaluation of quality measures. Prescribed dose should be evaluated at least once every 24 h and more often according to patient needs (Level V; Grade E).
- ✓ Recent data : CRRT dose lower than recommended by the KDIGO CPG default dose → adequate control of serum urea concentrations .
- ❑ **Effluent flow rate can be increased or decreased in response to changes in clinical, physiologic and/or metabolic status**
- ❑ Importantly, there are currently no data to support the concept that dynamic prescription improves surrogate or patient centered outcomes.


High solute control needs
Default zone
Low solute control needs
Patient A
Patient B
Patient C
CRRT dose (ml/kg/h)
40
25
20
10
CRRT start
1
2
3
4
Time (days)

- **In prescribing CRRT dose, additional parameters should be considered beyond urea clearance, such as acid–base and electrolyte homeostasis, nutrition, fluid balance and antimicrobial clearance**

What quality measures (quality indicators) should monitor dose and solute control in CRRT?

Metric	Definition	Calculation	Benchmark target
Dose (clearance)	This QM focuses on solute clearance to determine delivered dose using blood and effluent solute concentration. This QM provides an instantaneous estimate of filter efficacy (i.e., sieving coefficient). This QM can be serially measured to evaluate solute clearance and filter performance. The default solute is urea; however, this QM could be applied to additional solutes	QM = effluent (urea)/blood (urea)	≥0.80
Dose (ratio of delivered/ prescribed)	This QM focuses on the effluent volume delivered relative to prescribed dose. This measure would be calculated as the ratio of average effective delivered dose (time-averaged (24 h)) divided by prescribed dose	QM = average effective delivered dose/prescribed dose	≥0.80
Effective treatment time	This QM focuses on the total average time a patient receives treatment in a given 24 h period. This measure is based on time and would incorporate treatment interruptions that were planned and unanticipated. Initial benchmark target should be ≥20 h/day. Additional QMs related to contributors and response to unplanned interruptions are necessary (e.g., catheter function, circuit/filter clotting, anticoagulation)	QM = 24 – downtime (hours)	≥20
Solute control indicators	This QM focuses on the absolute and/or relative change in targeted solutes that represent a target of CRRT prescription	QM = $solute_{Day(x+1)}$/ $solute_{Day(x)}$	≤1.0
Circuit control indicators	This QM focuses on temporal trends in circuit and filter membrane pressures. These would specifically evaluate the pressure drop (P_{DROP}) and transmembrane pressure (TMP). These measures would indicate suboptimal clearance and risk of treatment interruption	QM = relative or absolute changes in P_{DROP} or TMP	P_{DROP}<? TMP<?

Blood Purif 2016;42:238–247

Where K is the clearance, QE is the effluent rate, CE is the effluent concentration, and CB is the blood concentration. K is expressed in mL/min

$$K = Q_E \times C_E / C_B \qquad (40.1)$$

where Qd is dialysate fluid rate, QR is replacement fluid rate, Qnet is the net fluid removal rate, and Quf is the total ultrafiltration volume. All are reported in mL/min. The effluent rate, which is also known as “dose” of CRRT, can be expressed in mL/h or as mL/kg/h. The recommended “dose” of RRT is at least 20 to 25 mL/kg/h

$$Q_E = Q_d + Q_R + Q_{net} \qquad (40.2)$$

$$Q_{uf} = Q_R + Q_{net} \qquad (40.3)$$

where σ is the sieving coefficient. For small molecules, the sieving coefficient approximates to 1. Using urea as the solute, equilibrium is achieved between CE and CB since the effluent rate is much smaller than the blood-flow rate and the solute size for urea is small (60 Da) (EQUATION 40.4). For instance, effluent rate is usually ranging 17 to 50 mL/min versus blood-flow rate around 200 to 300 mL/min. Therefore, the sieving coefficient for urea is 1. Another determinant of the sieving coefficient is the pore size of the hemodiafilter. TABLE 40.3 shows an example of the sieving coefficient of different molecules

$$\sigma = C_E / C_B \qquad (40.4)$$

$K = Q.eff \times C.eff / B.c$

$Q.eff = Q.d + Q.r + Q.net$

$Q.uf = Q.r + Q.net$

sieving coefficient = C.eff / C.b

CVVH (prefilter) : Diluting factor = Q.b / (Q.b + Q.r)

filtration fraction = Q.uf / (1-Hct).Q.b + pre filter Q.r

K : clearance
Q.eff : effluent rate
C.eff : effluent concentration
B.c : blood concentration
Q.R : Replacement fluid rate
Q.Net : net fluid removal
Q.uf : total UF volume

Wt : 70 kg , Hct = 30%
Mode : **CVVHD**
Qb :100 mL/min
Qd : 1.5 L/h
UF: 2 L

$$K = Q_E \times C_E / C_B$$

$$Q_E = Q_d + Q_R + Q_{net}$$
$$= 1{,}500 \text{ mL/h} + 0 + 83 \text{ mL/h}$$
$$= 1{,}583 \text{ mL/h}$$

$$K = (1{,}583 \text{ mL/h})\ (1) = 26 \text{ mL/min}$$

"Dose" is $(1{,}583 \text{ mL/h}) / 70 \text{ kg} = 23 \text{ mL/kg/h}$

$$FF = Q_{uf} / [(1 - \text{hematocrit})\ (Q_B)];\ Q_{uf} = Q_R + Q_{net}$$

$$Q_{uf} = 0 + 2 = 2 \text{ L/d or } 1.4 \text{ mL/min}$$

$$FF = 1.4 \text{ mL/min} / (1 - 0.3)\ (100 \text{ mL/min}) = 0.02 \text{ or } 2\%$$

Wt : 70 kg ; Hematocrit is 30%
Mode : **CVVH (post filter)**
Qb : 100 cc/min
Qr : 1.5 lit/h (post filter)
No UF

$$K = Q_E \times C_E / C_B$$

$$Q_E = Q_d + Q_R + Q_{net}$$
$$= 1{,}500 \text{ mL/h} + 0 + 0$$
$$= 1{,}500 \text{ mL/h}$$

$$K = (1{,}500 \text{ mL/h})\ (1) = 25 \text{ mL/min}$$

"Dose" is $(1{,}500 \text{ mL/h}) / 70 \text{ kg} = 21 \text{ mL/kg/h}$

$$FF = Q_{uf} / (1 - \text{hematocrit})\ (Q_B);\ Q_{uf} = Q_R + Q_{net}$$

$$Q_{uf} = 1{,}500 \text{ mL/h} + 0 = 1500 \text{ mL/h or } 25 \text{ mL/min}$$

$$FF = 25 \text{ mL/min} / [100 \text{ mL/min} \times (1 - 0.3)] = 0.36 \text{ or } 36\%$$

Wt : 70 kg ; Hct =30%
Mode : **CVVH (pre filter)**
QB : 100 cc/min
QR : 1.5 L/h
No UF

$K = Q_E \times C_E / C_B$

$$Q_E = Q_d + Q_R + Q_{net}$$
$$= 1{,}500 \text{ mL/h} + 0 + 0$$
$$= 1{,}500 \text{ mL/h}$$

Use dilution factor $= Q_B / (Q_B + Q_R)$

Therefore, $K = [Q_E \times C_E/C_B] \times [Q_B / (Q_B + Q_R)]$

$K = (1{,}500 \text{ mL/h}) \times 1 \times (6{,}000 \text{ mL/h}) / (6{,}000 \text{ mL/h} + 1{,}500 \text{ mL/h}) = 1{,}200 \text{ mL/h}$ or 20 mL/min or 17 mL/kg/h

$FF = Q_{uf} / [(1 - \text{hematocrit}) (Q_B) + \text{prefilter } Q_R]$; $Q_{uf} = Q_R + Q_{net}$

$Q_{uf} = 1{,}500 \text{ mL/h} + 0 = 1{,}500 \text{ mL/h}$ or 25 mL/min

$FF = 25 \text{ mL/min} / [100 \text{ mL/min} \times (1 - 0.3) + 25 \text{ mL/min}] = 0.26$ or 26%

A 60 yo man ; CVVH (Post filter) ; Hct : 30%
Qb : 100 cc /min
Qef : 1 lit/h
BUN : 90 mg/dl
FUN : 60 mg/dl
20 hours → filter clotted

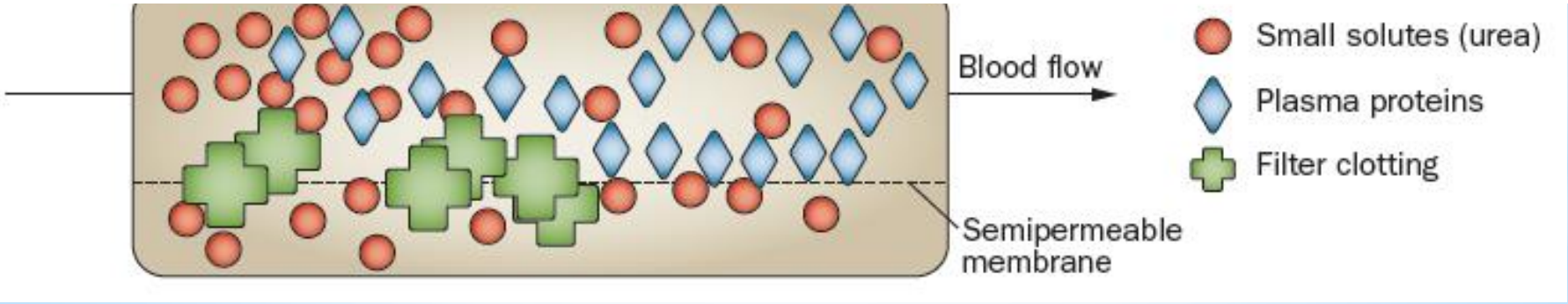
FUN/BUN < 0.8
≥ 20 hours

- **Kurea = 1000 mL/h * 60/90 (0.66)**
  = 660 mL/h
  = 11 ml/min.
  (13 mL/kg/hr)

Factors Influencing CRRT Clearances :

- **Patient factors**
- **Treatment factors :**
  - **Catheter**
  - **Filter :**
    - Down time due to filter clotting **(major reason for reduced RRT dose)**
    - Concentration polarization →reduces UF rate and the filtrate concentrations of various medium / large sized proteins
    - Convection – Diffusion interactions
  - **Time out of therapy**

Prescribed dose = (Qr + Qd + Qnet) ≠ Delivered dose = (Qr + Qd + Qnet) x S



Concentration polarization, membrane fouling and filter clotting **decrease the FUN/BUN ratio** over time

Mendu *et al. BMC Nephrology* (2017) 18:351
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BMC Nephrology

RESEARCH ARTICLE Open Access

Non-tunneled versus tunneled dialysis catheters for acute kidney injury requiring renal replacement therapy: a prospective cohort study

Mallika L. Mendu[1,5*], Megan F. May[1], Arnaud D. Kaze[1], Dionne A. Graham[2], Salena Cui[1], Margaret E. Chen[1], Naomi Shin[3], Ayal A. Aizer[4] and Sushrut S. Waikar[1]

- A prospective cohort study ; over a 16-month period ; 154 patients initiated on AKI-RRT / at an academic hospital (Brigham and Women's Hospital , Boston
- **KDIGO : using NTDCs rather than TDCs for vascular access in AKI (level of evidence, 2D)**

Only 2 of 80 TDCs had mechanical omplications, compared to 92 of 140 NTDCs

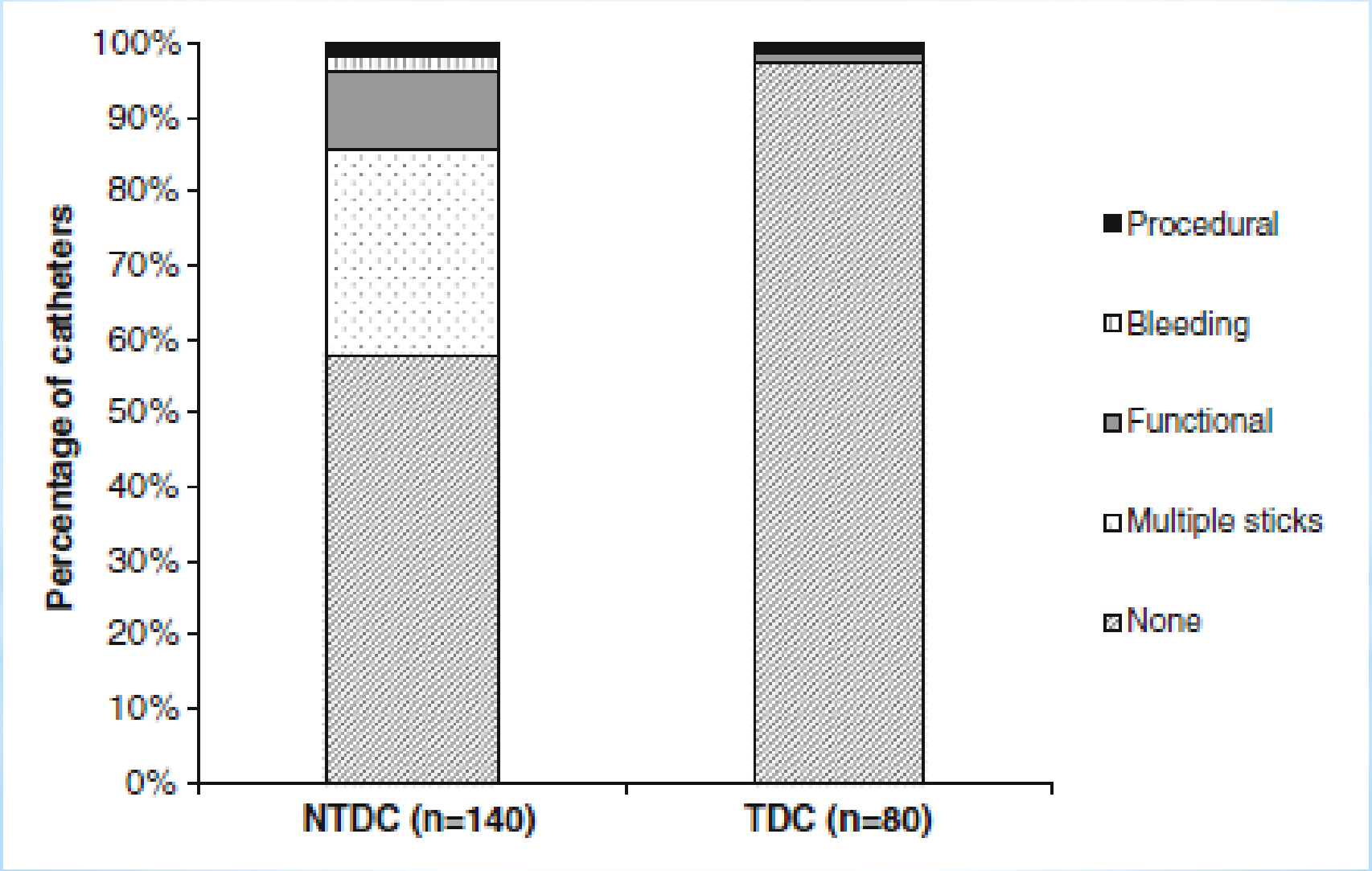

Table 3 Complications in non-tunneled versus tunneled dialysis catheters used for AKI requiring renal replacement therapy

Complication outcome	Adjusted rate ratio,[a] NTDC vs TDC (95% CI)	*p*-value
Blood culture		
Cultures drawn per catheter	2.1 (1.7–2.8)	<0.001
Positive cultures drawn per catheter	1.4 (0.6–3.4)	0.41
Mechanical complications		
Mechanical complications (excluding multiple sticks)	13.6 (2.9–63.0)	0.001
Mechanical complications (including multiple sticks)	69.1 (16.6–288.2)	<0.001
All complications		
Positive cultures and mechanical complications (excluding multiple sticks)	3.3 (1.6–6.8)	<0.001
Positive cultures and mechanical complications (including multiple sticks)	12.5 (6.5–24.0)	<0.001
Number of catheters per patient	1.8 (1.2–2.6)	0.002

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Prescribed clearance **overestimated** the actual delivered clearance by **23.8%**. This gap between prescribed and delivered clearance was related to the **decrease in filter function assessed by the FUN/BUN ratio**.

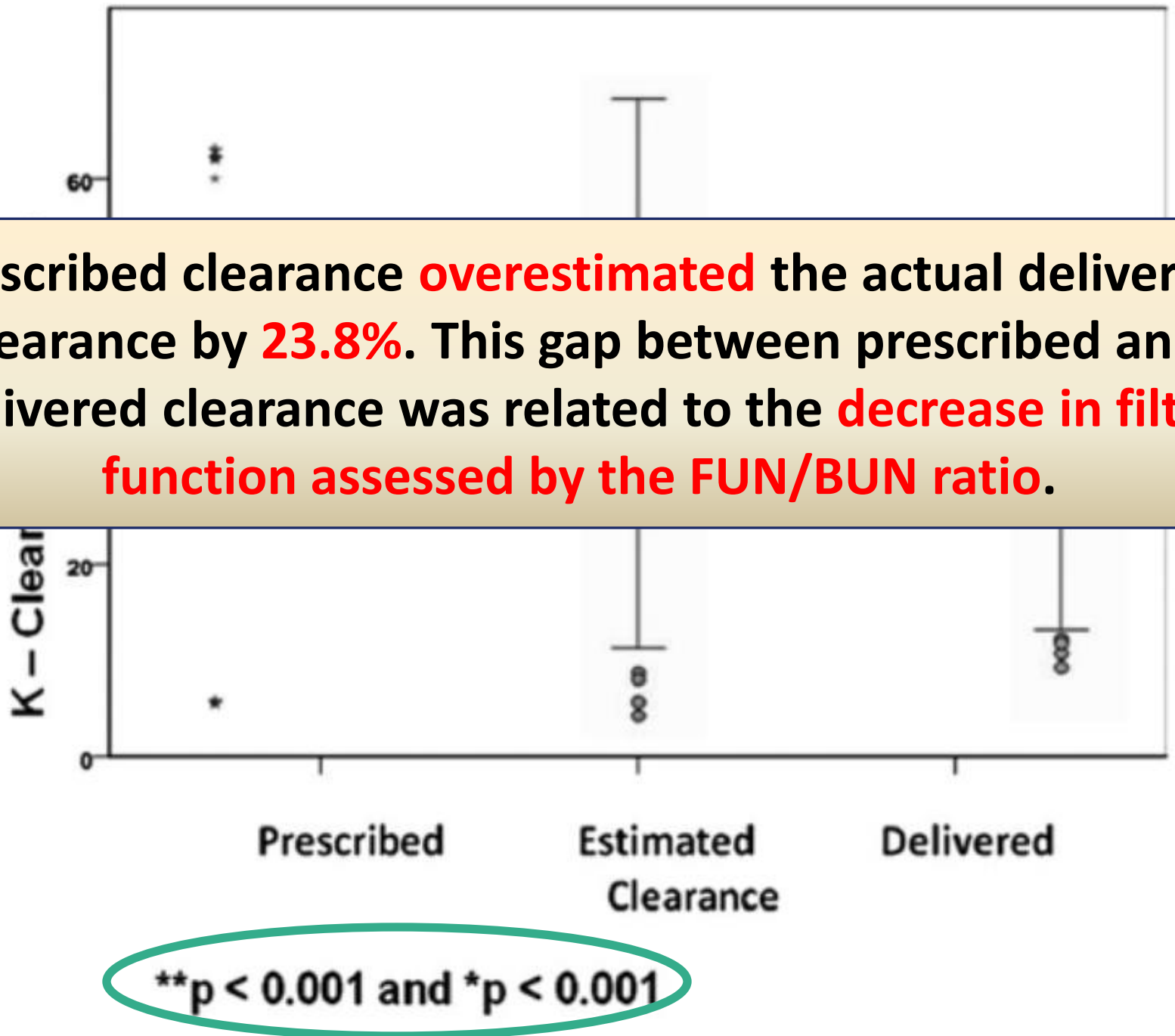

Table 3. Reasons for stopping CRRT

Reasons	Number of Filters	Percentage (%)	FUN/BUN Ratio
filter leak	1	0.63	0.745
low sieving concentration	12	7.5	0.86 (0.79 to 1.0)
polarization			

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."


خسته نباشید