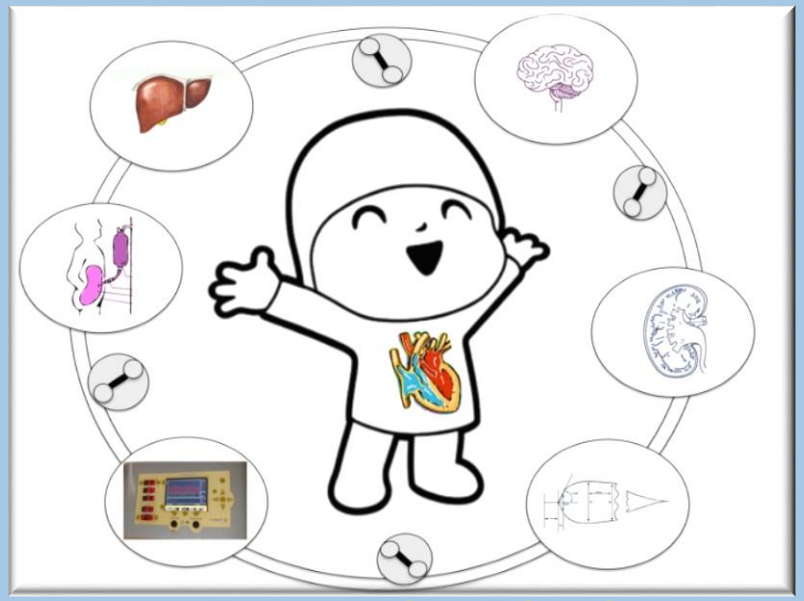
Principali problemi tecnici e clinici

CRRT
Questione di EQUIPE!

Videoconferenza LIVE per
INFERMIERI
NEFROLOGI
INTENSIVISTI ...
e tutti i Medici in Formazione Specialistica!
XI Edizione



15-16 giugno 2020

Zaccaria Ricci

Dipartimento Medico Chirurgico
di Cardiologia Pediatrica

Bambino Gesù
OSPEDALE PEDIATRICO

Health-e-Child

Comune di Roma

Information Society Technologies

The NEW ENGLAND JOURNAL of MEDICINE

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

The VA/NIH Acute Renal Failure Trial Network*

Table 4. Summary of Complications Associated with Study Therapy.*

Event	Intensive Strategy (N=563)	Less-Intensive Strategy (N=561)	P Value
	no. of patients (%)		
Any serious adverse event†	287 (51.0)	280 (49.9)	0.72
Not related to study therapy	207 (72.1)	202 (72.1)	
Possibly or probably related to study therapy	48 (16.7)	51 (18.2)	
Definitely related to study therapy	32 (11.1)	27 (9.6)	
Nonfatal only‡	137 (47.7)	128 (45.7)	
Catheter-related complications			
Insertion-related complications	28 (5.0)	31 (5.5)	0.68
Late catheter-related complications	48 (8.5)	38 (6.8)	0.27
Hypotension			
Requiring vasopressor support	81 (14.4)	56 (10.0)	0.02
Requiring discontinuation of treatment	55 (9.8)	49 (8.7)	0.55
Requiring other intervention	212 (37.7)	168 (29.9)	0.006
Other treatment-related complications			
Any nonhypotensive complication	216 (38.4)	194 (34.6)	0.19
Electrolyte disturbance	144 (25.6)	116 (20.7)	0.05
Hypokalemia	42 (7.5)	25 (4.5)	0.03
Hypophosphatemia	99 (17.6)	61 (10.9)	0.001
Other	99 (17.6)	85 (15.2)	0.27

COMPLICANZE DURANTE CRRT

CLINICHE

- Ipotensione
- Coagulazione
- Anemia
- Ipotermia
- Diselettrolitemie
- Perdita di soluti
- Complicazioni correlate all'accesso vascolare

TECNICHE

- Errori nella somm.ne della terapia
- Errori di bilancio
- Interfaccia macchina-operatore
- Altre complicanze "elettroniche"

Original Paper

Blood Purification

Blood Purif 2015;39:333–339
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Incidence of Adverse Events during Continuous Renal Replacement Therapy

Abbasali Akhoundi[a] Balwinder Singh[b] Myriam Vela[a] Sanjay Chaudhary[b]
Myles Monaghan[a] Gregory A. Wilson[c] John J. Dillon[a] Rodrigo Cartin-Ceba[b]
John C. Lieske[a] Ognjen Gajic[b] Kianoush Kashani[a, b]

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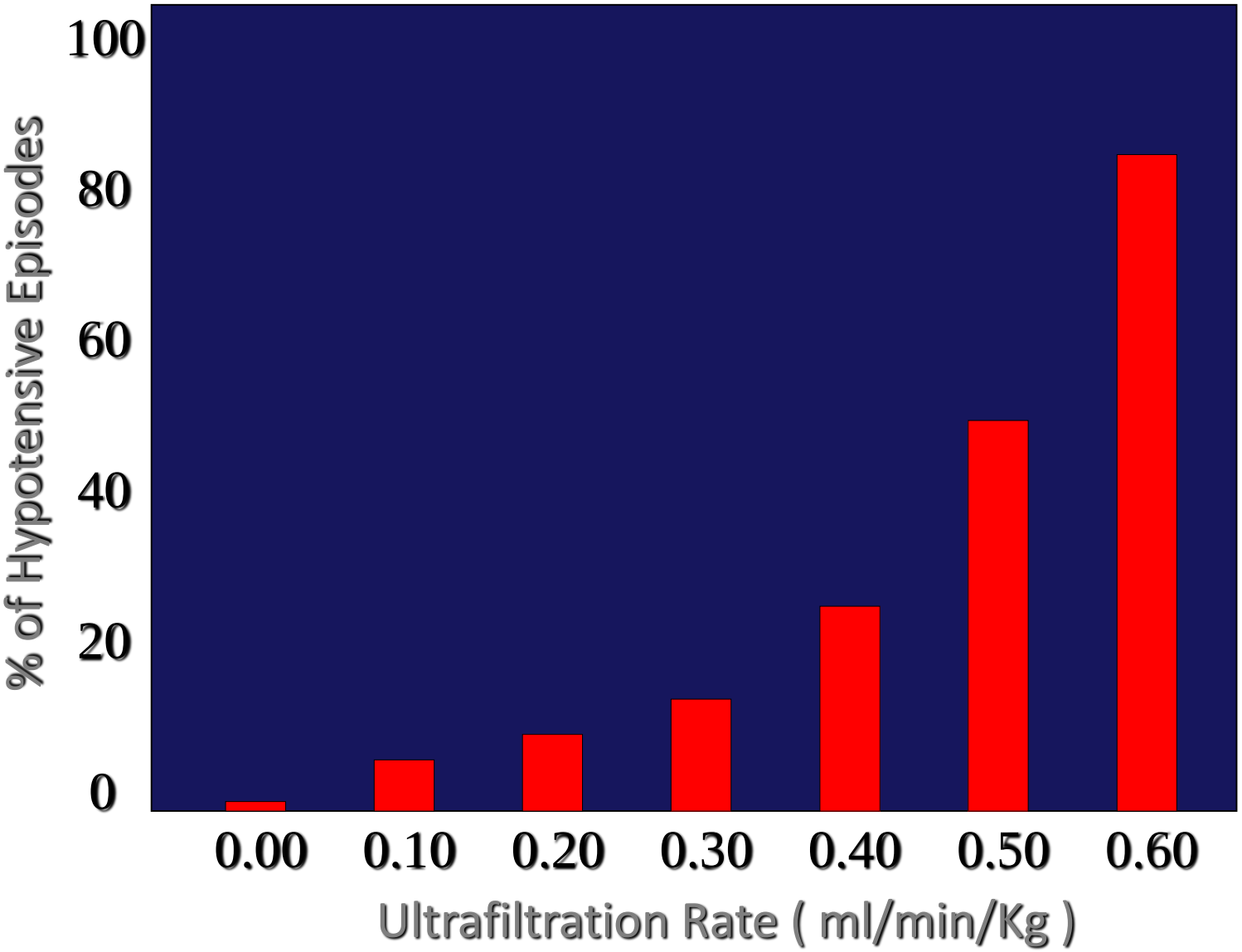
[c]Department of Anesthesiology, Mayo Clinic, Rochester, Minn., USA

Table 2. Adverse events

Catheter-related complication, n (%)	225 (38)
Bleeding	134 (23)
Arterial puncture	6 (1)
Hematoma	17 (2.85)
Other	71 (11.93)
Line-related infection*	30 (5)
SAEs, n (%)	573 (97)
First-hour hypotension	258 (43)
Significant hypothermia (<35 °C)	259 (44)
New onset anemia-Hgb <10 g/dL	179 (31)
New onset thrombocytopenia (<50% baseline) with baseline platelet >150,000	73 (13)
New onset thrombocytopenia (<50% baseline) with baseline platelet <150,000	143 (26)
Arrhythmia, n (%)	484 (81)
Sinus tachycardia	306 (51)
Atrial fibrillation	64 (11)
Atrial flutter	6 (1)
Ventricular tachycardia	14 (2)
Sinus bradycardia	43 (7)
Ventricular fibrillation	19 (3)
Asystole	20 (3)
Others	12 (2)
CPR	28 (5)

FREQUENZA DI IPOTENSIONE IN HD

Ronco et Al, Int J. Artif Organs, 3, 169-174, 1988



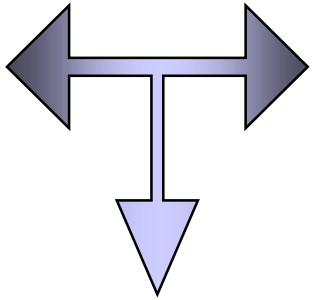
Pz di 70 Kg con AKI: sessione dialitica di 24 ore

24 hour input

Blood - plasma infusions
Drugs and Medications
Parenteral Nutrition
Volume administration

24 hour output

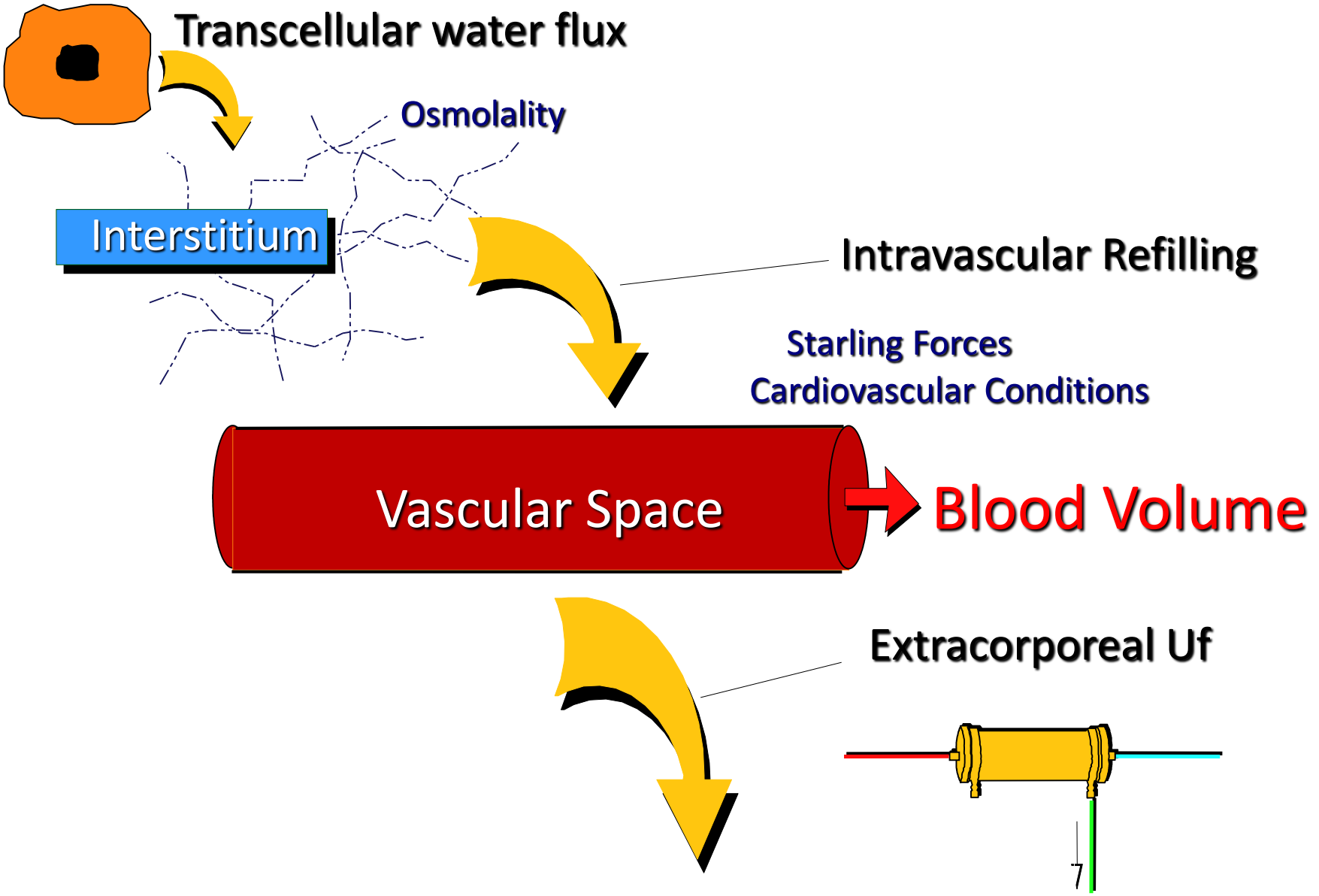
Urine output (=0)
Intestinal fluid losses
Insensible losses
Other fluid losses



Ultrafiltration required = 4000 ml

Short Daily HD 3 hours	Ext.Daily HD 8 hours	CVVH 24 hours
23 ml/min 0.4 ml/min/Kg	8.3 ml/min 0.1 ml/min/Kg	2.5 ml/min 0.03 ml/min/Kg

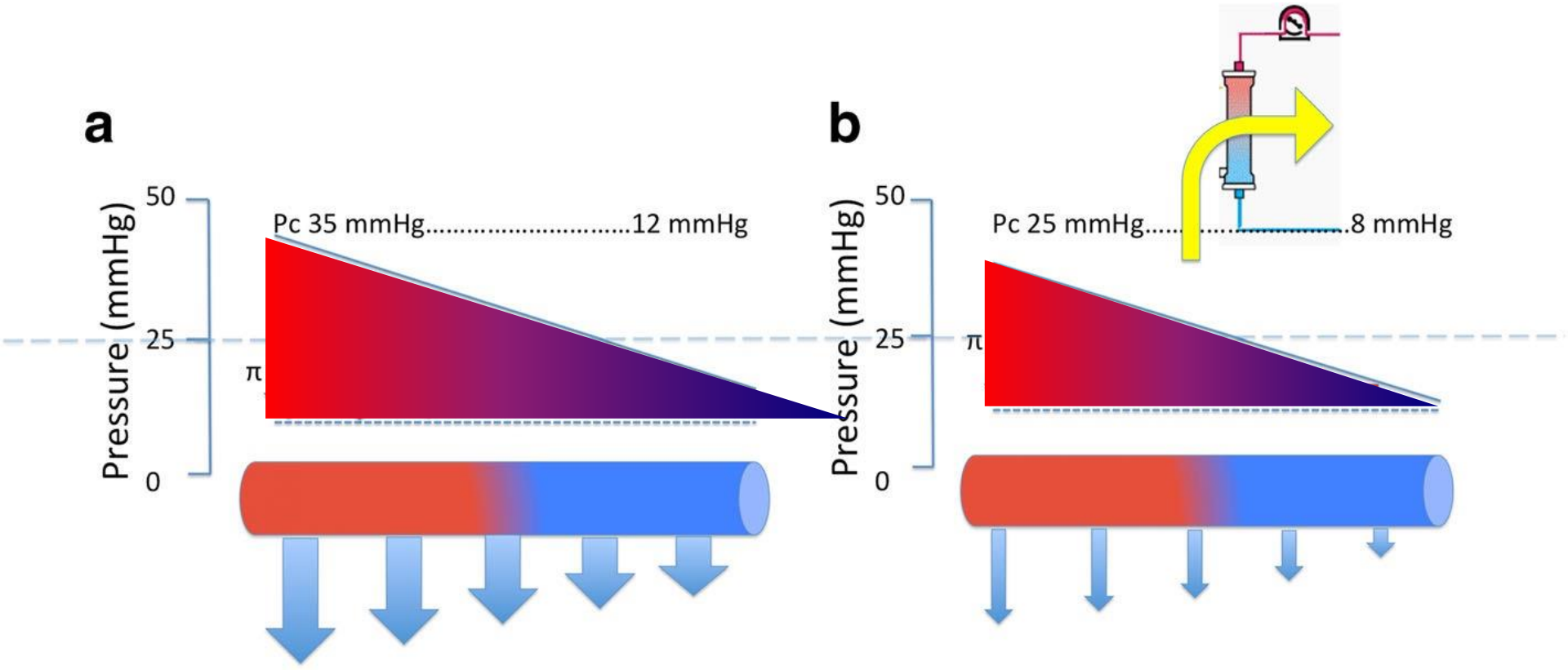
BLOOD VOLUME = Ultrafiltration – Refilling



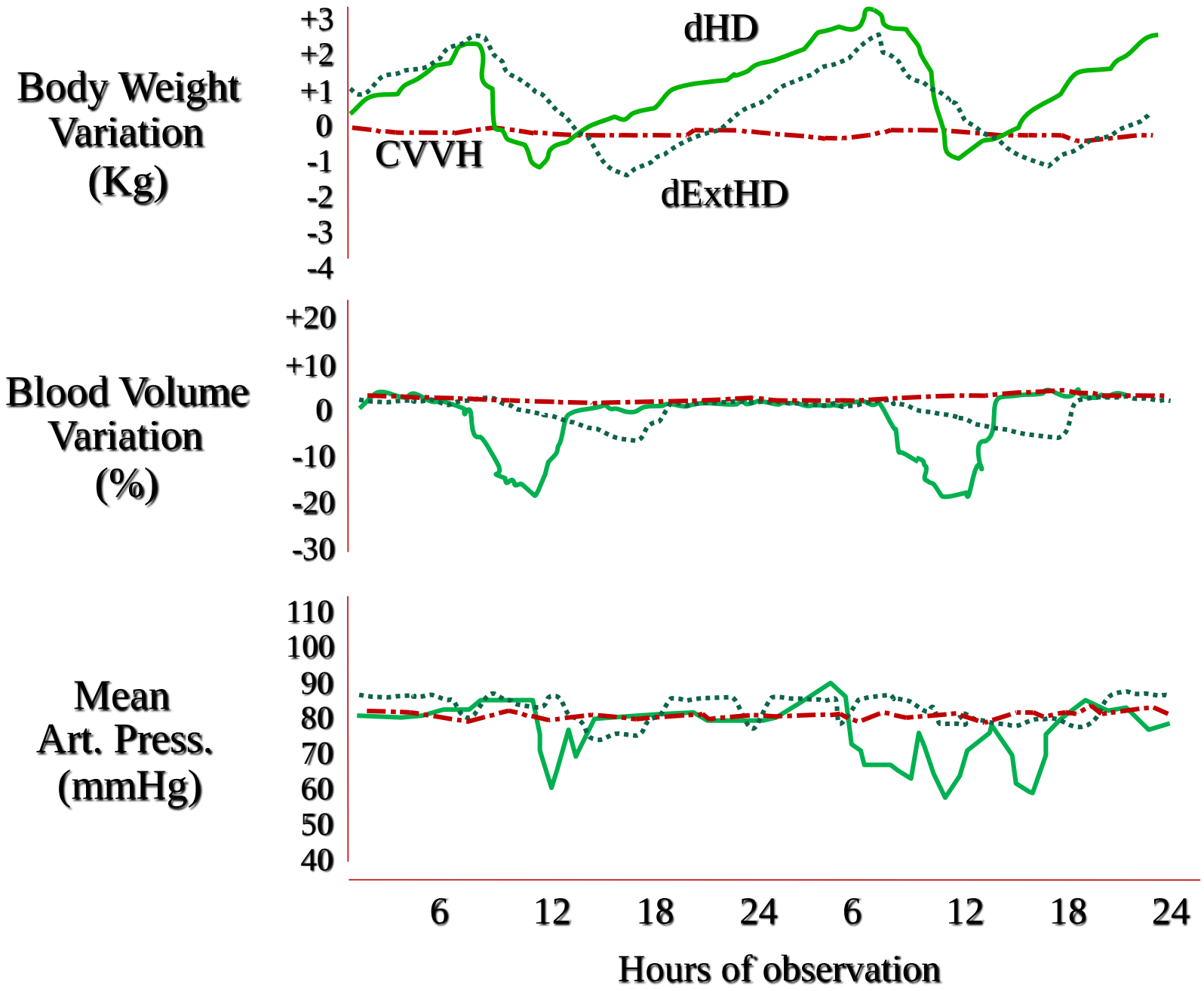
LETTER Open Acces

Cardiac output and CVP monitoring… to guide fluid removal

Matthieu Legrand[1,2,3*], Sabri Soussi[1] and François Depret[1,2]



LA RIDUZIONE DELLA PRESSIONE ATRIALE DESTRA A PARITA' DI FLUSSO (PORTATA CARDIACA=RITORNO VENOSO) E' LA DIMOSTRAZIONE CHE IL PROCESSO DI ULTRAFILTRAZIONE E' EFFICACE


Body Weight Variation (Kg)
+3
+2
+1
0
-1
-2
-3
-4
dHD
CVVH
dExtHD
Blood Volume Variation (%)
+20
+10
0
-10
-20
-30
Mean Art. Press. (mmHg)
110
100
90
80
70
60
50
40
6
12
18
24
6
12
18
24
Hours of observation

The NEW ENGLAND JOURNAL of MEDICINE

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

The VA/NIH Acute Renal Failure Trial Network*

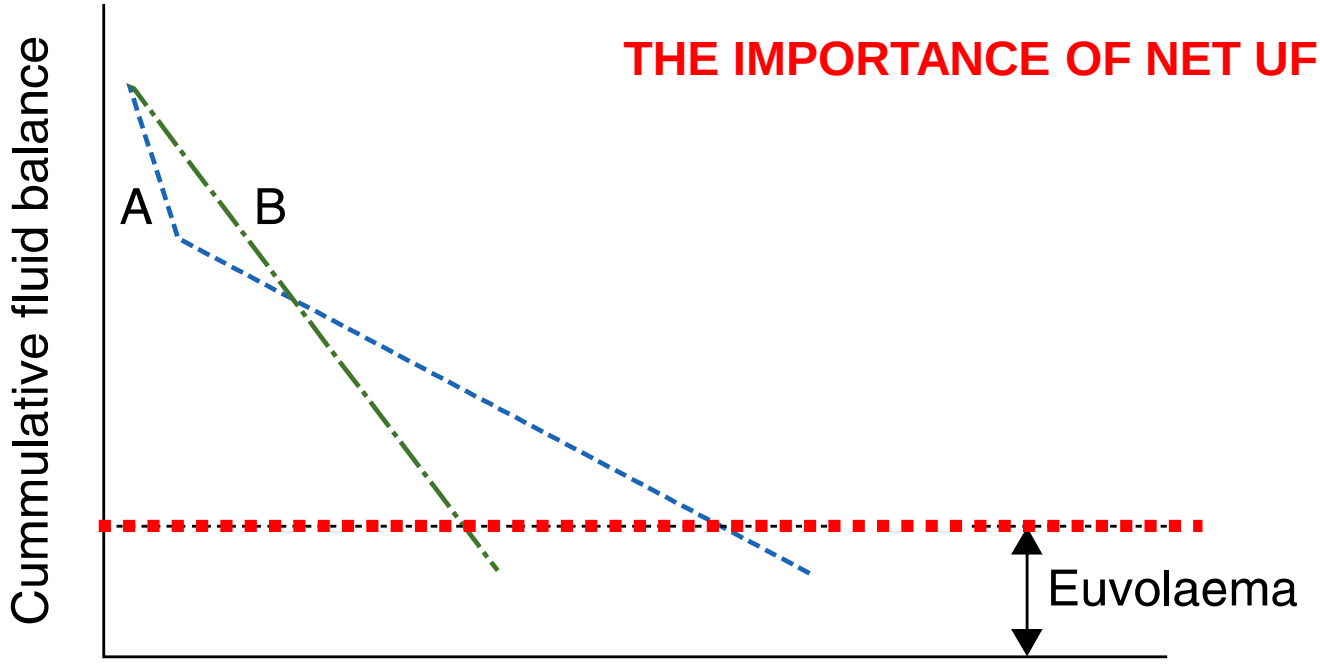
	IHD	SLED	IUF	CRRT
Net UF (L/day)	1.8-2.1	1.3-1.4	2.1-2.7	2.7-2.9
(mL/h)	300-700	150-300	150-200	100-110

VA/NIH Acute Renal Failure Trial Network, NEJM 2008

Indications and management of mechanical fluid removal in critical illness

M. H. Rosner[1†], M. Ostermann[2†*], R. Murugan[3], J. R. Prowle[4], C. Ronco[5], J. A. Kellum[3], M. G. Mythen[6] and A. D. Shaw[7] for the ADQI XII Investigators Group

BJA 2014



Rapid early fluid removal may be indicated in cardio-renal syndrome (A) (i.e. pulmonary oedema). Patients with single organ renal failure (B) may tolerate more rapid fluid removal than those with AKI complicating hemadynamic instability (C) or septic shock (D).

CAUSE DI SBILANCIO FLUIDICO DURANTE CRRT

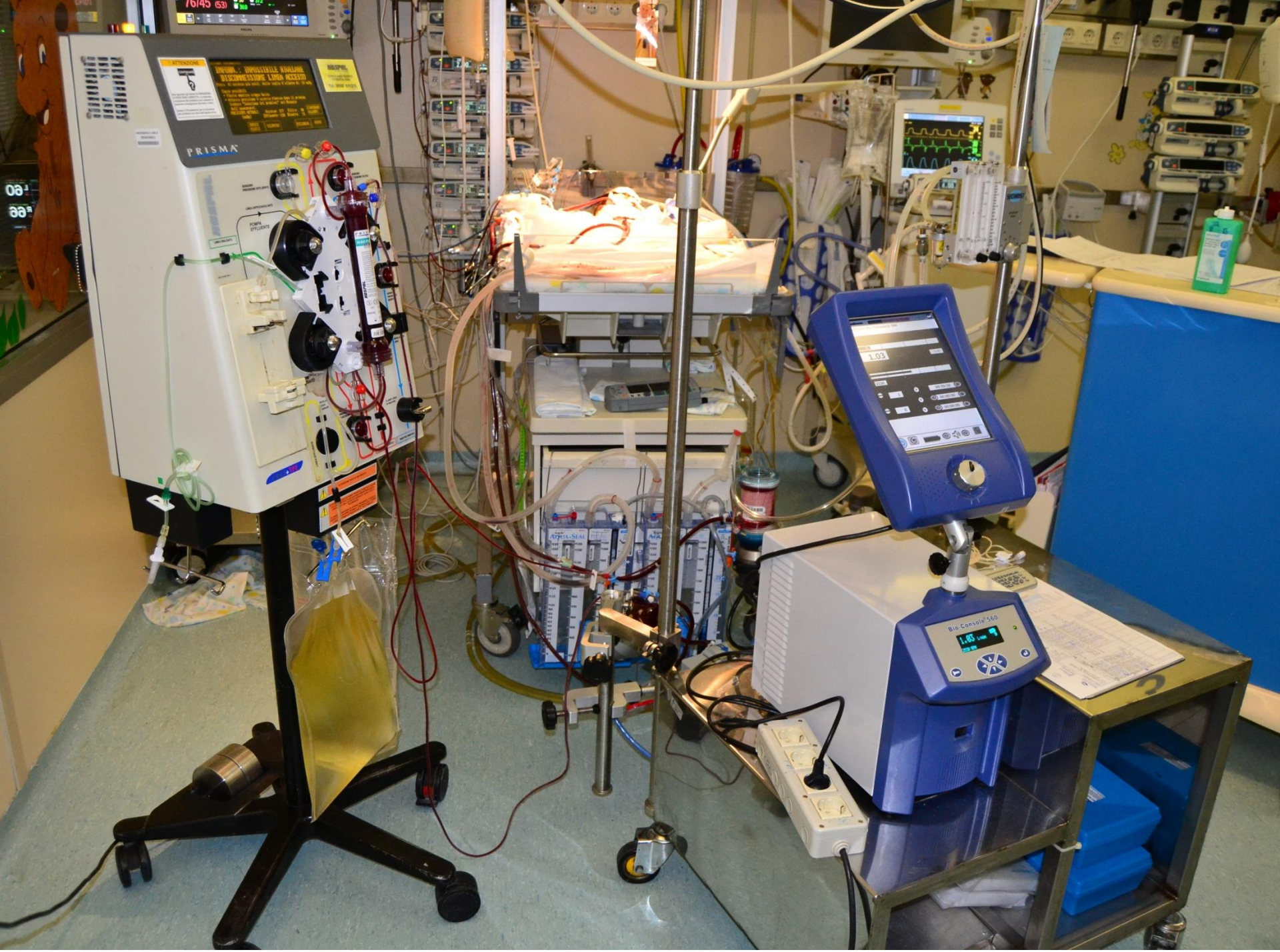
Fluid Imbalance

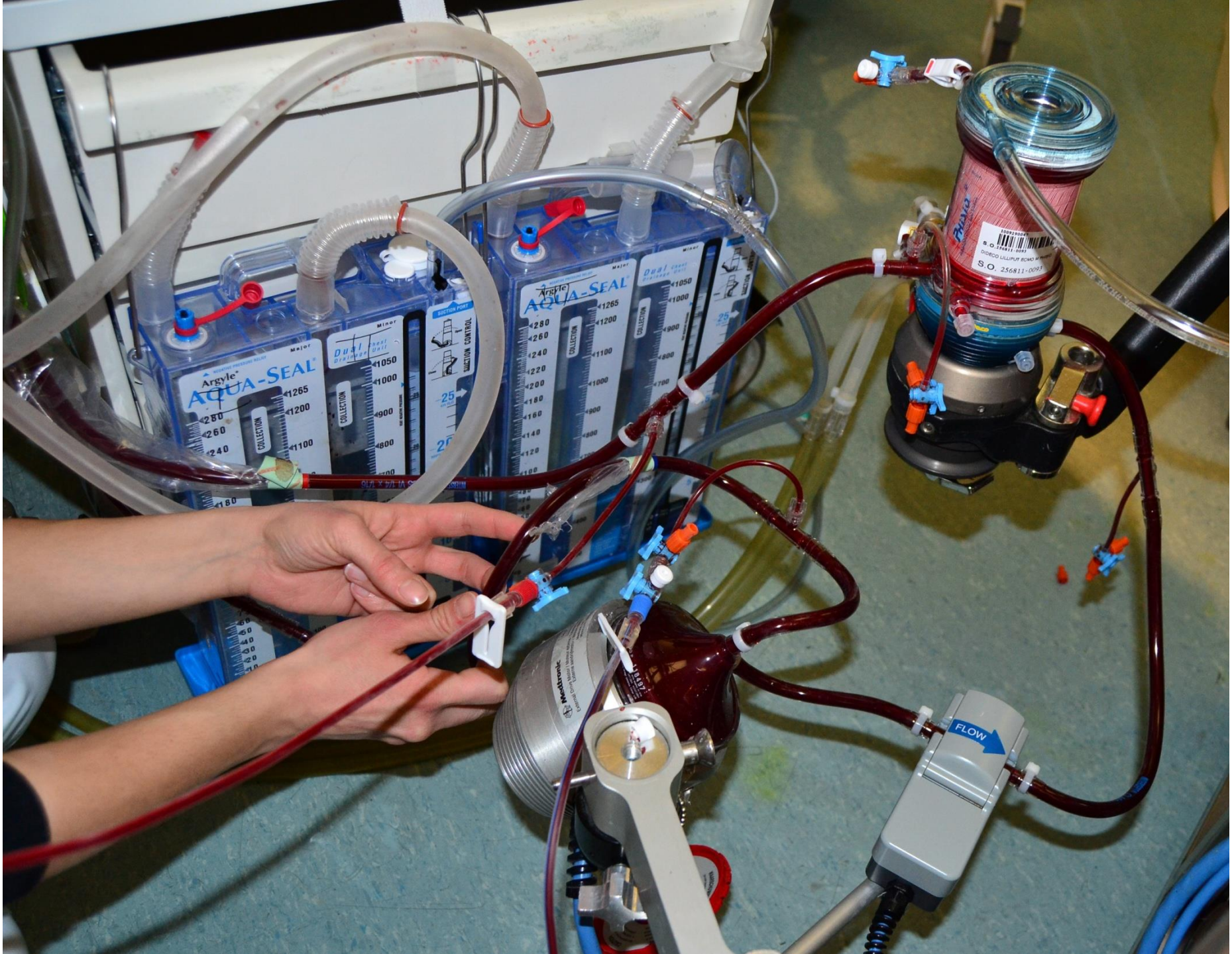
Positive

- Insufficient fluid removal
- Fluid Gain

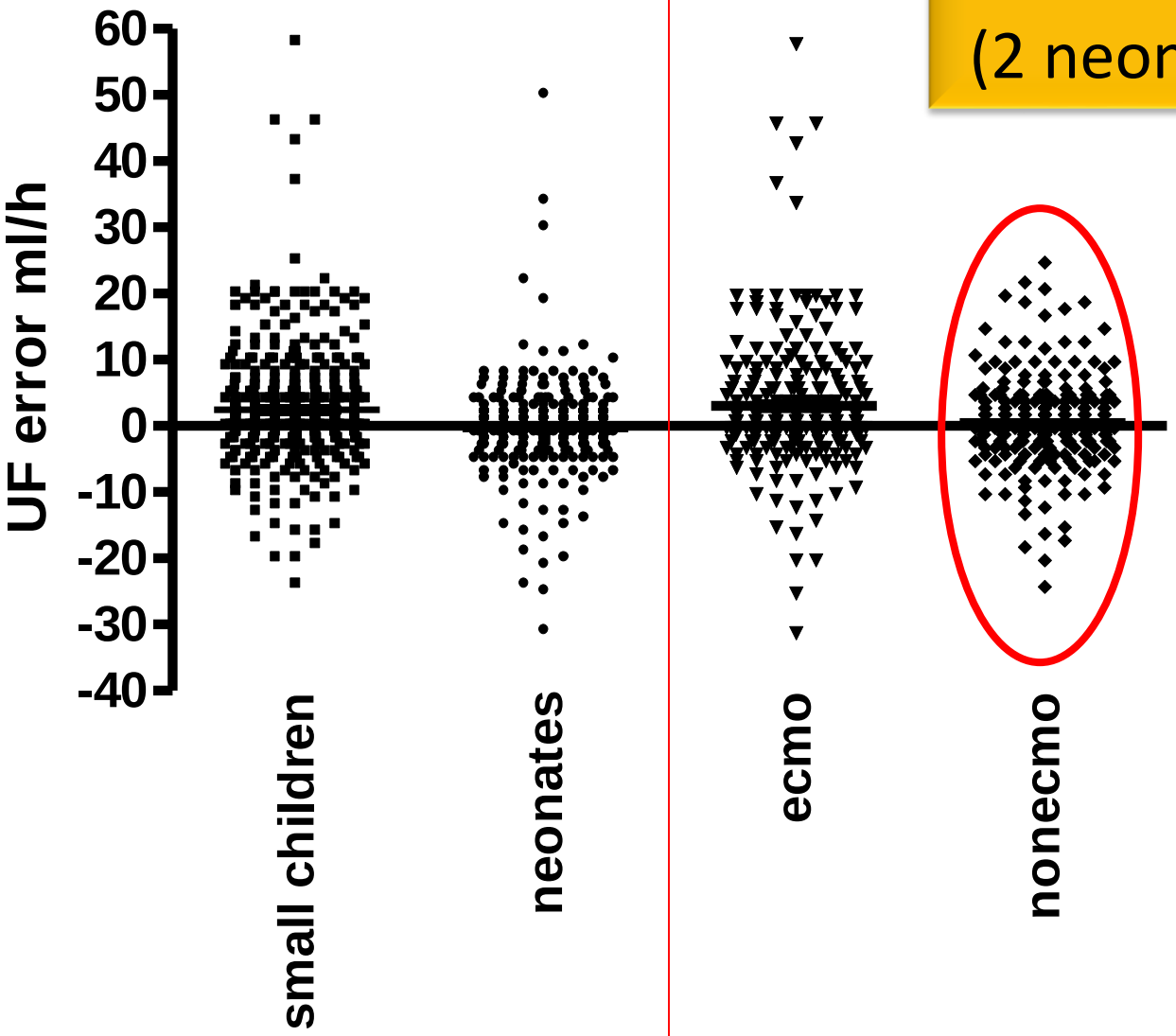
Negative

- Absolute volume (Total Uf)
- Relative Volume (Uf rate)
- TECH ERROR (THRESHOLD)


PRISMA
Bio-Console 560


Argyle
AQUA-SEAL
Dual
Major
Minor
COLLECTION
SUCTION CONTROL
SUCTION PORT
Medtronic
FLOW
S.O. 256811-0093

N = 4 pts with AKI
(2 neonates +2 children)



1 neonate and 1 child required pCRRT+ECMO

1 neonate a 1 child required pCRRT alone

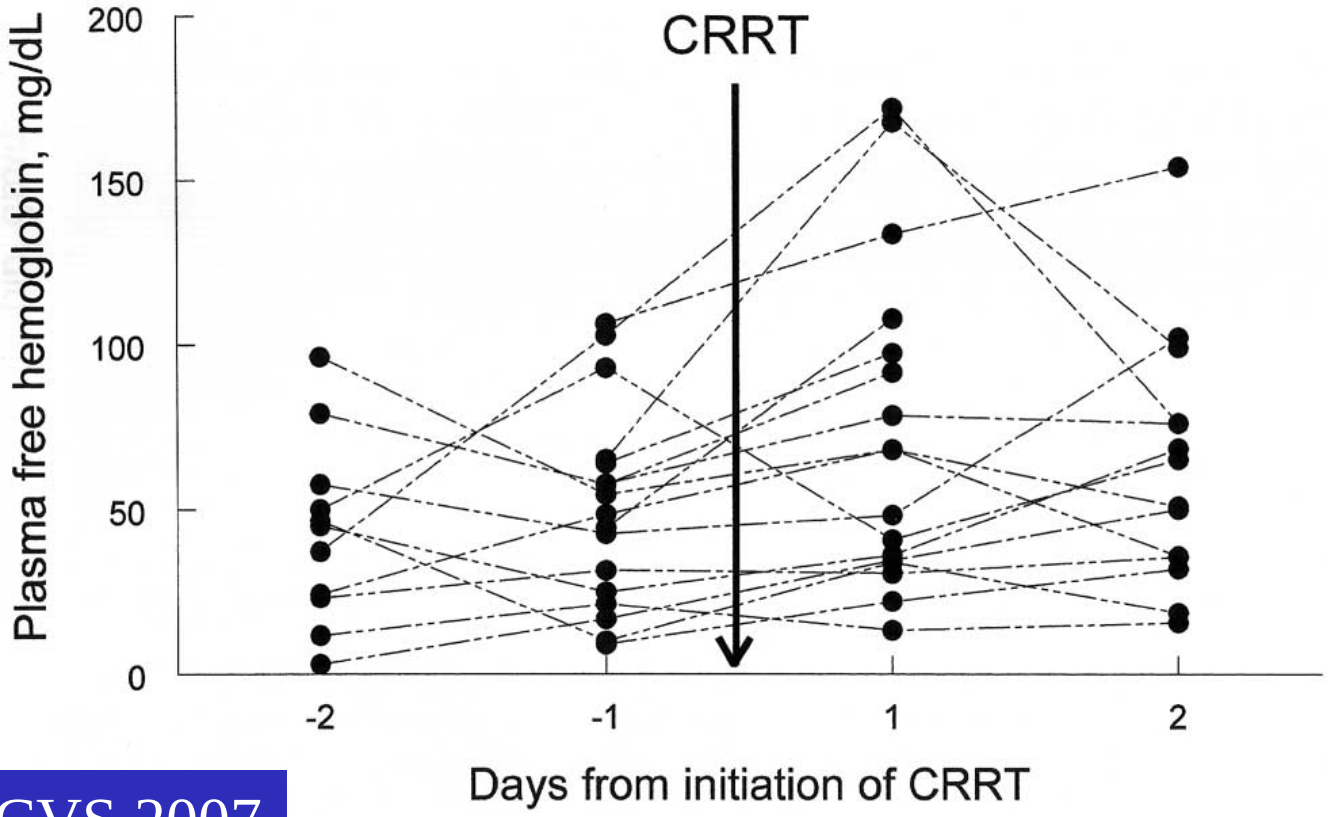
ANEMIA

- Fiber clotting results in blood loss
- Blood loss from vascular access (example: arterial catheter in CAVH/ CAVH/ CAVHD)
- Mechanical hemolysis from shear stress/roller pumps on RBC in extracorporeal circuit

IN CHILDREN, DEDICATED CIRCUITS WITH LOW PRIMING VOLUMES ARE MANDATORY

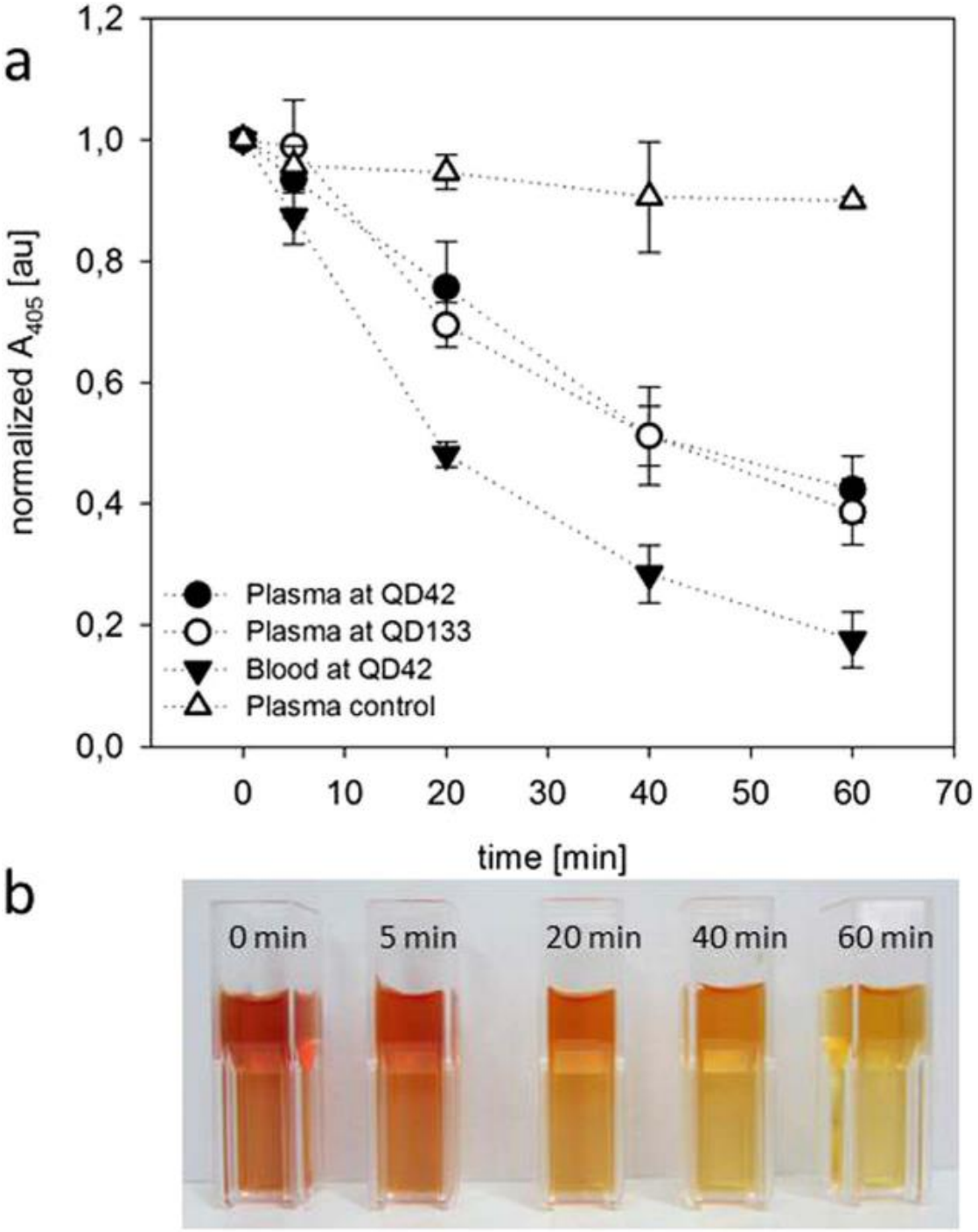
ANEMIA

- No study currently evaluated the incidence of hemolysis during CRRT and its clinical impact



Betrus, ATCVS 2007

UNA POTEN) ALTO CUT OFF



Hulko et al,
Scient Rep 2015

Cucchiari et al. BMC Nephrology (2018) 19:250
https://doi.org/10.1186/s12882-018-1051-x

BMC Nephrology

CASE REPORT Open Access

High cut-off membrane for in-vivo dialysis of free plasma hemoglobin in a patient with massive hemolysis

David Cucchiari[1*], Enric Reverter[2], Miquel Blasco[1], Alicia Molina-Andujar[1], Adriá Carpio[2], Miquel Sanz[2], Angels Escorsell[2], Javier Fernández[2] and Esteban Poch[1]

Table 1 Treatment data and CPH concentrations 30′, 24 h and 48 h after CRRT start

	30 min	24 h	48 h
C_{In} (g/L)	4,24	4,33	3,72
C_{Out} (g/L)	4,23	4,19	3,66
C_D (g/L)	0,37	0,1	0,07
Sieving Coefficient	0,087	0,023	0,018
Clearance (ml/min)	2,87	0,76	0,62
Q_b (ml/min)	250	250	250
Q_d (ml/min)	33	33	33
Q_e (ml/Kg/h)	28,2	29	29
UF (ml/h)	0	50	50

C_{In} CPH concentration at the arterial side, *C_{Out}* CPH concentration at the venous side, *C_D* CPH concentration at dialysate side, *Q_b* blood flow, *Q_d* dialysate flow, *Q_e* effluent flow, *UF* UltraFiltration rate

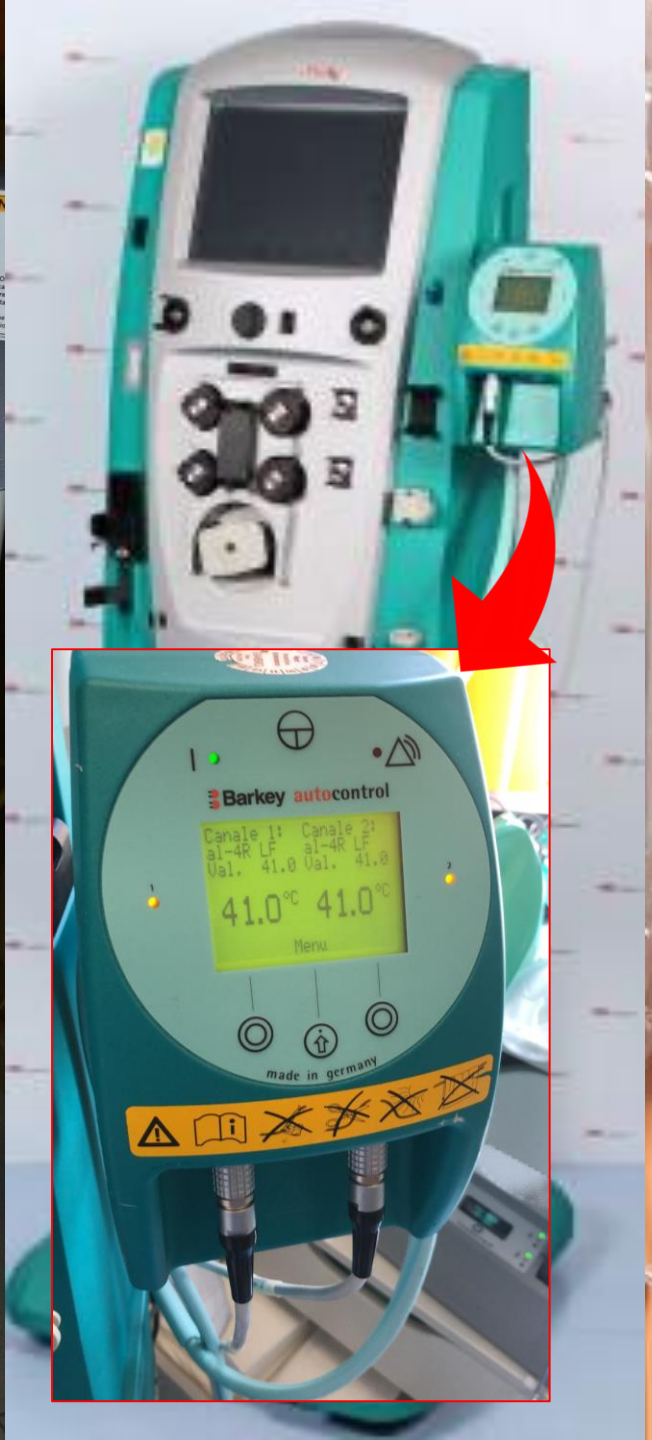
✓ HCO cut-off: 60 kD
✓ Hb tetramer 62 kD
✓ Hb dimer 30 kD
(present with CPH <[1] g/L)

IPOTERMIA

- Extracorporeal radiant heat exchange
- Administration of large volumes of unwarmed substitution fluid may result in cooling of patient → **hypothermia**

- Heat loss of 750 kcal / day, thereby increasing the patient's daily energy requirements and need for a warming blanket


PRISMA
STATO
ATTENZIONE
CONTINUARE
SENSORE PRESSIONE EFFLUENTE
SENSORE PRESSIONE FILTRO
POMPA EFFLUENTE
POMPA REINFUSIONE
SENSORE PRESSIONE RIENTRO
POMPA DIALISATO
POMPA SANGUE
CLAMP LINEA DI RIENTRO


Barkey autocontrol
41.0°C 41.0°C
Menu
made in germany

ALTERAZIONI ELETTROLITICHE

- Hypophosphatemia (especially with high dose therapies
  - May be associated with prolonged weaning (??Weakening of respiratory muscles)
- Hypokalemia
- Hypocalcemia (when using regional citrate anticoagulation)
- Hypercalcemia (with prolonged use of 3.5 Ca solutions)
- Hyperglycemia with use of PD solutions
- Human error (using the wrong solution)

Original Paper

Blood Purification

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Received: August 14, 2014
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Incidence of Adverse Events during Continuous Renal Replacement Therapy

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[a]Division of Nephrology and Hypertension, Department of Internal Medicine, Mayo Clinic, Rochester, Minn.,
[b]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Mayo Clinic, Rochester, Minn.,
[c]Department of Anesthesiology, Mayo Clinic, Rochester, Minn., USA

Table 3. Electrolyte abnormalities

	Baseline median (IQR)	Incidence, n (%)	Values median (IQR)	Clinically significant[a], n (%)
Sodium, mmol/l	139 (134–143)			
Hyponatremia		148 (25)	137 (135–139)	4 (0.6)
Hypernatremia		170 (29)	144 (142–146)	20 (3)
Potassium, mmol/l	4.5 (3.9–5.1)			
Hypokalemia		269 (45)	3.6 (3.4–3.9)	25 (4)
Hyperkalemia		155 (26)	4.7 (4.4–5.2)	44 (7)
Total calcium, mg/dl	8.7 (7.9–9.4)			
Hypocalcemia		114 (19)	9.35 (8.6–10.3)	11 (3)
Hypercalcemia		207 (35)	10.7 (9.6–11.7)	48 (8)
Ionized calcium, mg/dl	4.53 (4.13–4.85)			
Hypocalcemia		547 (92)	4.05 (3.69–4.37)	131 (22)
Hypercalcemia		369 (62)	5.89 (5.41–6.33)	136 (23)
Phosphorus, mg/dl	5.4 (4.1–6.8)			
Hypophosphatemia		346 (58)	2.3 (1.9–2.9)	201 (34)
Hyperphosphatemia		395 (66)	5.2 (4.3–6.6)	263 (44)
Magnesium, mg/dl	2.2 (1.9–2.5)			
Hypomagnesaemia		190 (32)	1.8 (1.7–1.9)	1 (0.1)
Hypermagnesemia		231 (39)	2.4 (2.2–2.6)	2 (0.3)

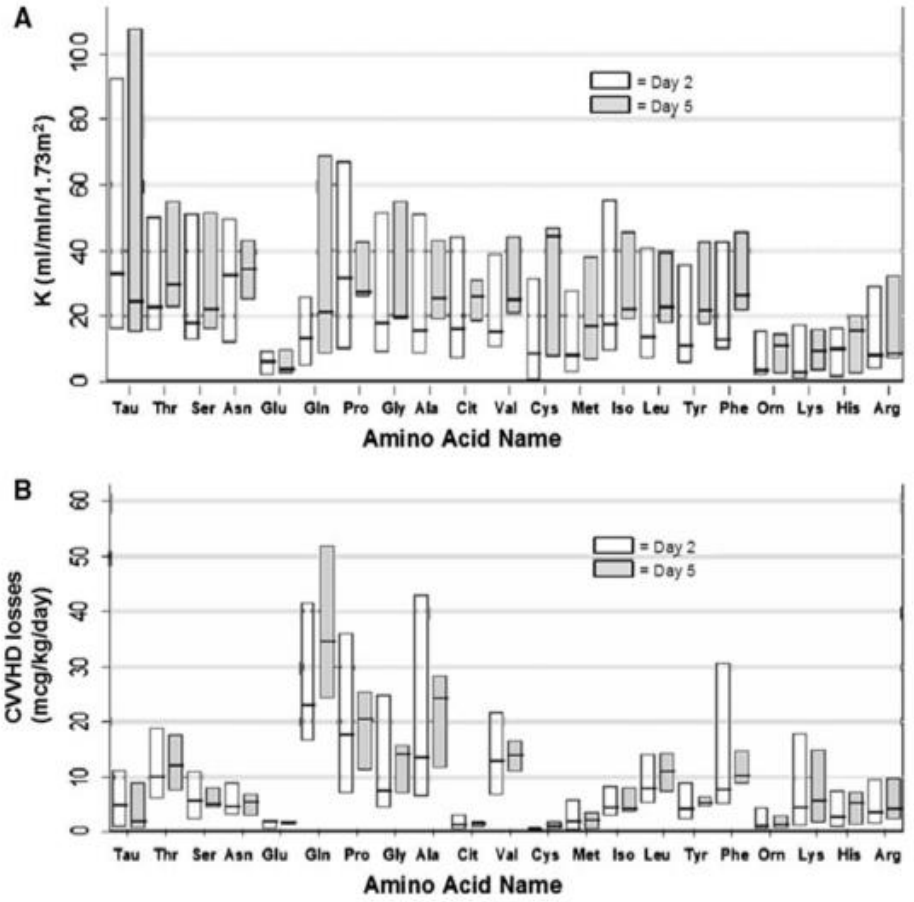
PERDITA DI AMINOACIDI

- Dialysate/ ultrafiltrate protein losses as high as 1.3 g/L with CRRT outputs of up to 50 L/day = protein losses up to 65 g/day
- Mean dialysate/ultrafiltrate protein concentration = 4 mg/dL (Biuret method)
- Protein losses were higher during convection based CVVH than CVVHDF
- Amount of protein loss also dependent on serum protein concentration
- Not yet well-studied with high volume CRRT (HVHF, PHVHF)

PERDITA DI AMINOACIDI

In standard clinical practice, CRRT overdose is a potential detrimental side effect of pediatric CRRT

Amino acid clearances ranged from 2.8 to 51.1 ml/min per 1.73 m2. CVVHD losses corresponded to 20% of intake.



Pediatric Nephrology
https://doi.org/10.1007/s00467-019-04211-z

BRIEF REPORT

Feeding modality is a barrier to adequate protein provision in children receiving continuous renal replacement therapy (CRRT)

Molly Wong Vega[1] &Marisa Juarez Calderon[1] &Naile Tufan Pekkucuksen[1] &Poyyapakkam Srivaths[1] &
Ayse Akcan Arikan[1,2]

Pediatr Nephrol

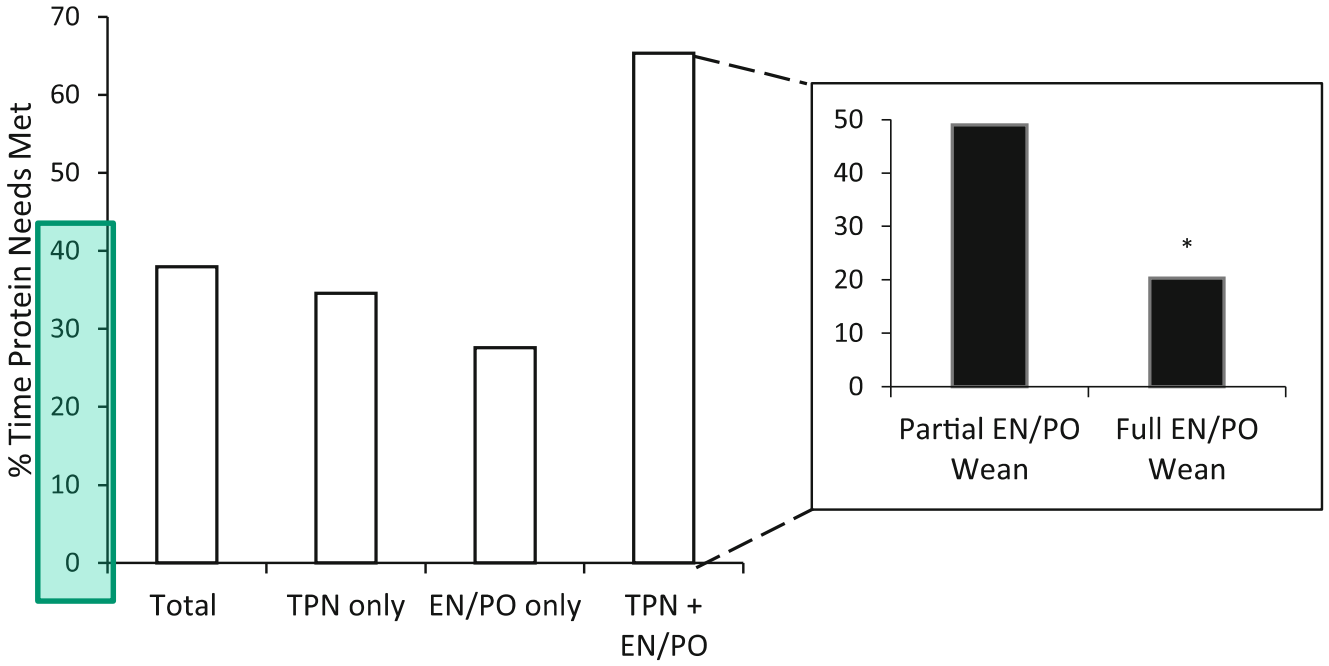


Fig. 1 Percentage of time meeting protein goals during CRRT by feeding modality. Initial data reported as total, further reported by only PN, only EN, or combination of PN and EN. Combination PN and EN group then divided by those whom were partially weaned from PN and maintained on combination versus those whom were fully weaned from PN to receive only EN. EN enteral nutrition, TPN total parenteral nutrition, PO by mouth. *$p < 0.01$

Farmaci: proprietà che determinano l'entità della rimozione con le terapie sostitutive

- Legame proteico
- Volume di distribuzione (Vd)
- Peso molecolare (PM)
- Idrosolubilità e carica elettrica
- Volume e conformazione della molecola

Proprietà dei farmaci: volume di distribuzione (Vd)

- I farmaci ad alto legame tissutale sono caratterizzati da un Vd elevato (amfotericina B: 4 L/Kg)

- Per i farmaci con Vd elevato (>2 L/Kg) la quantità relativa di farmaco presente nel plasma è modesta rispetto agli altri compartimenti:

- Vd ≤ 1 L/Kg → $Cl_{EXTRACORPOREA}$ significativa
- Vd > 2 L/Kg → $Cl_{EXTRACORPOREA}$ irrilevante

Proprietà dei farmaci: Peso Molecolare (PM)

- La maggior parte dei farmaci di comune impiego nel paziente critico hanno un PM ≤ 500 Da

- Vancomicina: PM = 1448 Da

- Le membrane di impiego comune in CRRT, sono caratterizzate da elevata porosità e permeabilità idraulica e non costituiscono una barriera al trasporto convettivo/diffusivo della frazione libera di farmaci a PM anche superiore a 1500 Da

Quali sono le caratteristiche ideali per la dializzabilità di un farmaco?

- ridotto legame proteico (> frazione libera del farmaco)
- basso peso molecolare (< 1500 Daltons)
- ridotto volume di distribuzione (<1 L/Kg)
- ⇑ idrosolubilità

Parametri farmacocinetici, SC e rimozione farmaci in CVVH

Farmaco	Escrez. Renale	Fraz. libera (%)	Vd ($L\ Kg^{-1}$)	PM (Da)	SC	Rimozione RRT
Amikacina	95%	>95%	0.22	586	0.95	S
Amfotericina B	5-10%	10%	4	926	0.35	N
Cefepime	85%	84%	0.3	481	0.72	S
Ceftazidime	60-85%	83%	0.28-0.40	547	0.90	S
Ceftriaxone	30-65%	10%	0.12-0.18	553	0.20	<< altri beta-lattamici
Ciprofloxacina	50-70%	60-80%	2.5	331	0.70	S
Fluconazolo	70%	88%	0.70	306	0.88	particolarmente ↑
Gentamicina	95%	>95%	0.23	478	0.81	S
Imipenem/Cilast	20-70 / 60%	79-87% / 56%	0.22 / 0.24	317/380	0.90/0.75	S
Meropenem	65%	98%	0.35	437	1.0	S
Piperacillina/ Tazobactam	75-90 / 65%	70% / 78%	0.25 / 0.21	540/322	0.82	S (Piperacillina > Tazob.)
Teicoplanina	40-60%	10-40%	0.5-1.2	1885	0.05	modesta
Vancomicina	90-100%	50-90%	0.47-1.1	1448	0.70-0.80	S

Diagnostic Microbiology and Infectious Disease 82 (2015) 92–103

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2015

How can we ensure effective antibiotic dosing in critically ill patients receiving different types of renal replacement therapy?

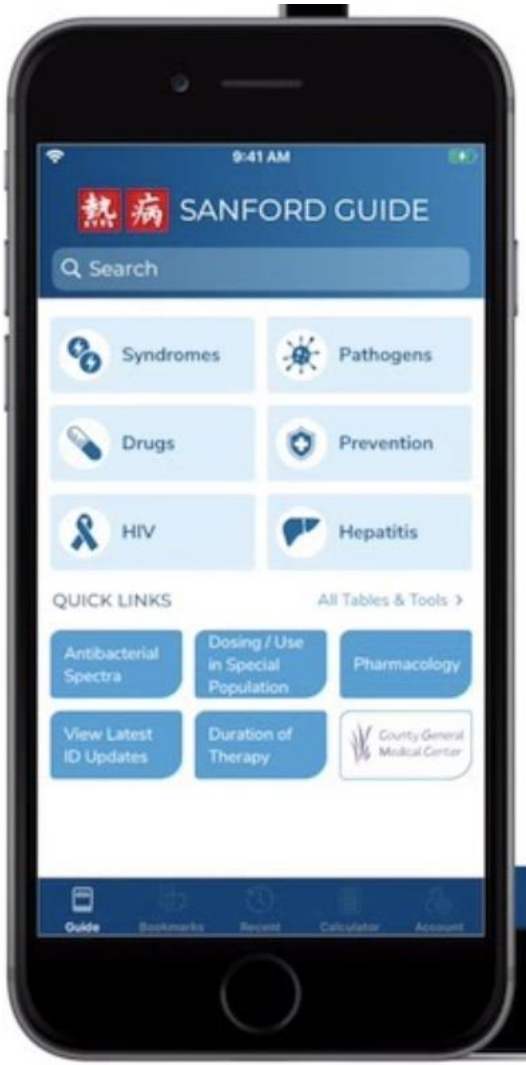
Janattul-Ain Jamal [a], Bruce A. Mueller [b], Gordon Y.S. Choi [c], Jeffrey Lipman [a,d], Jason A. Roberts [a,d,*]

[a] Burns Trauma and Critical Care Research Centre, The University of Queensland, Herston, QLD, Australia
[b] Department of Clinical Social and Administrative Sciences, College of Pharmacy University of MI, Ann Arbor, USA
[c] Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong
[d] Royal Brisbane and Women's Hospital, Herston, QLD, Australia

Table 1
Pharmacokinetic parameters of different classes of antibiotics in critically ill patients receiving different renal replacement therapy modalities.

Drug/(Reference)	Type of RRT/No. of patients (n)	RRT settings			Dose	Pharmacokinetic parameters[a]						
		Qb (mL/min)	Qe (mL/min)	Filter material/ surface area (m^2)		C_{max} (mg/L)	C_{max}/C_{t0} (mg/L)	V_d (L)	AUC_{0-T} (mg.h/L)	Cl_{total} (mL/min)	Cl_{RRT} (mL/min)	S_c
Aminoglycosides												
Amikacin* (Akers et al., 2011)	CVVH (n = 12)	NA	41.7 ± 18.7	Polysulfone (1.4, 1.5)	15 mg/kg 24H	29.1 ± 14.5	1.5 ± 1.6	70.0 ± 88.3	214.8 ± 113.8[b]	146.7 ± 148.3	NA	NA
Amikacin (Taccone et al., 2011)	CVVHDF (n = 13)	150.0	61.0	Polyacrylonitrile/ Polysulfone (NA)	25 mg/kg (first dose)	70.0[b] (38.3–94.6)	9.6[b] (4.1–29.9)	35.0[b,f] (15.4–283.5)	NA	88.2[b,f] (7.0–231.0)	NA	NA
Amikacin (D'Arcy et al., 2012)	CVVHDF (n = 5)	200.0	50.0–66.7	Polyacrylonitrile (0.6)	0.3–1.5 g 12–54H	48.2[b] (7.6–68.3)	3.0[b] (2.1–16.1)	31.4 ± 3.3	NA	58.0 ± 12.3	47.7 ± 6.8	0.8 ± 0.
Gentamicin (Petejova et al., 2013a)	CVVH (n = 7)	200.0	67.5	Polysulfone (1.4/1.8)	0.24 g (LD), 0.24–0.32 g 24H	8.8[b] (5.6–12.5)	0.5[b] (0.4–1.3)	42.3[b] (39.6–49.5)	NA	61.2[b] (44.1–107.1)	28.8[b] (27.9–30.6)	0.8

QUESTE GUIDE IN GENERE NON TENGONO IN CONSIDERAZIONE DELL'IMPATTO DELLE DIVERSE CLEARANCE CON CRRT



Variability of antibiotic concentrations in critically ill patients receiving continuous renal replacement therapy: A multicentre pharmacokinetic study*

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CCM 2012

- Wide variability in trough concentrations: 6.7-fold for meropenem, 3.8-fold for piperacillin, 10.5-fold for tazobactam, 1.9-fold for vancomycin, and 3.9-fold for ciprofloxacin.

- Overall, **15% of dosing intervals did not meet predetermined minimum therapeutic target concentrations**, 40% did not achieve the higher target concentration, and, during **10% of dosing intervals, antibiotic concentrations were excessive**.

CONCLUSIONI

- Le complicanze (cliniche) durante terapie continue sono frequenti ma…
- …RARAMENTE possono raggiungere elevati livelli di gravità!
- Specialmente quando sono gestite da un team adeguatamente preparato: monitoraggio accurato della tecnica, procedure mediche e infermieristiche standardizzate e specificamente protocollate.
- Ipotensione: soprattutto allo start terapia e in caso di Uf_{netta} eccessiva
- Clearance: alcune importanti sostanze vengono rimosse, più spesso di quanto si pensi in eccedenza (elettroliti e aminoacidi, antibiotici)