Continuous Renal Replacement Therapy: ci sono novità?

Cosimo Chelazzi, MD, PhD

The 10 false beliefs in adult critical care nephrology

WHAT'S NEW IN INTENSIVE CARE

FALSE BELIEFS

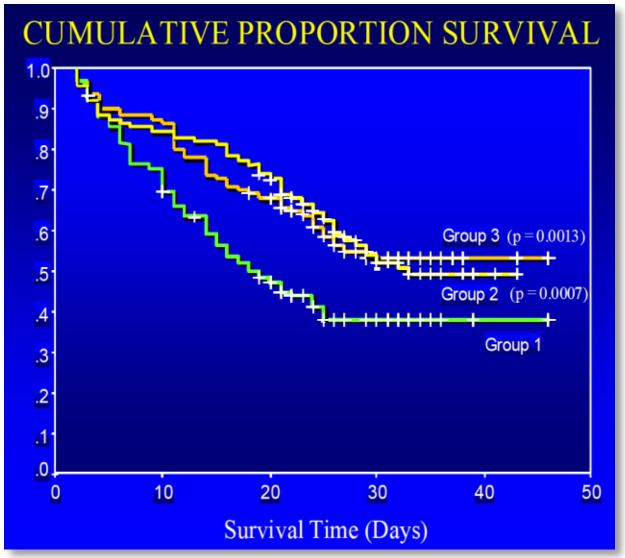
- ATN is the main histopathologic finding in AKI
- Decreased RBF is the leading cause of AKI during sepsis
- Effluent flow equals RRT dose
- Extracorporeal blood purification is a "cure" for sepsis
- Restoration of creatinine levels after AKI implies full recovery
- High blood flow rates in RRT cause hemodynamic instability
- To wean my anuric patient from RRT I could try to force diuresis
- IJV is the best access for RRT
- Fluid challenge is ALWAYS recommended in patients with oliguria
- MAP is the principal hemodynamic target in patients with AKI

TRUE CONCEPTS

- ATN is an uncommon histopathologic finding in AKI
- Septic AKI may occur despite increased RBF
- Effluent flow overestimates RRT dose
- Source control is the "cure" for sepsis
- Restoration of creatinine levels is a biased measure of full recovery
- Net UF and rapid osmolality decrease may cause hemodynamic instability in RRT
- Before attempting to wean my anuric patient from RRT I have to wait for spontaneous diuresis
- Right IJV and femoral veins have similar performances as RRT accesses
- Fluid challenge is ONLY recommended in fluid responsive patients with oliguria and/or hypotension
- Mean and Diastolic PP are reliable hemodynamic targets in patients with AKI

Zaccaria Ricci[1*], Stefano Romagnoli[2] and Claudio Ronco[3,4]

- There is a positive relationship between **treatment dose** and **outcome** in patients with acute kidney injury → patients receiving a higher dose had better survival than those randomized to 20 ml/kg/h.



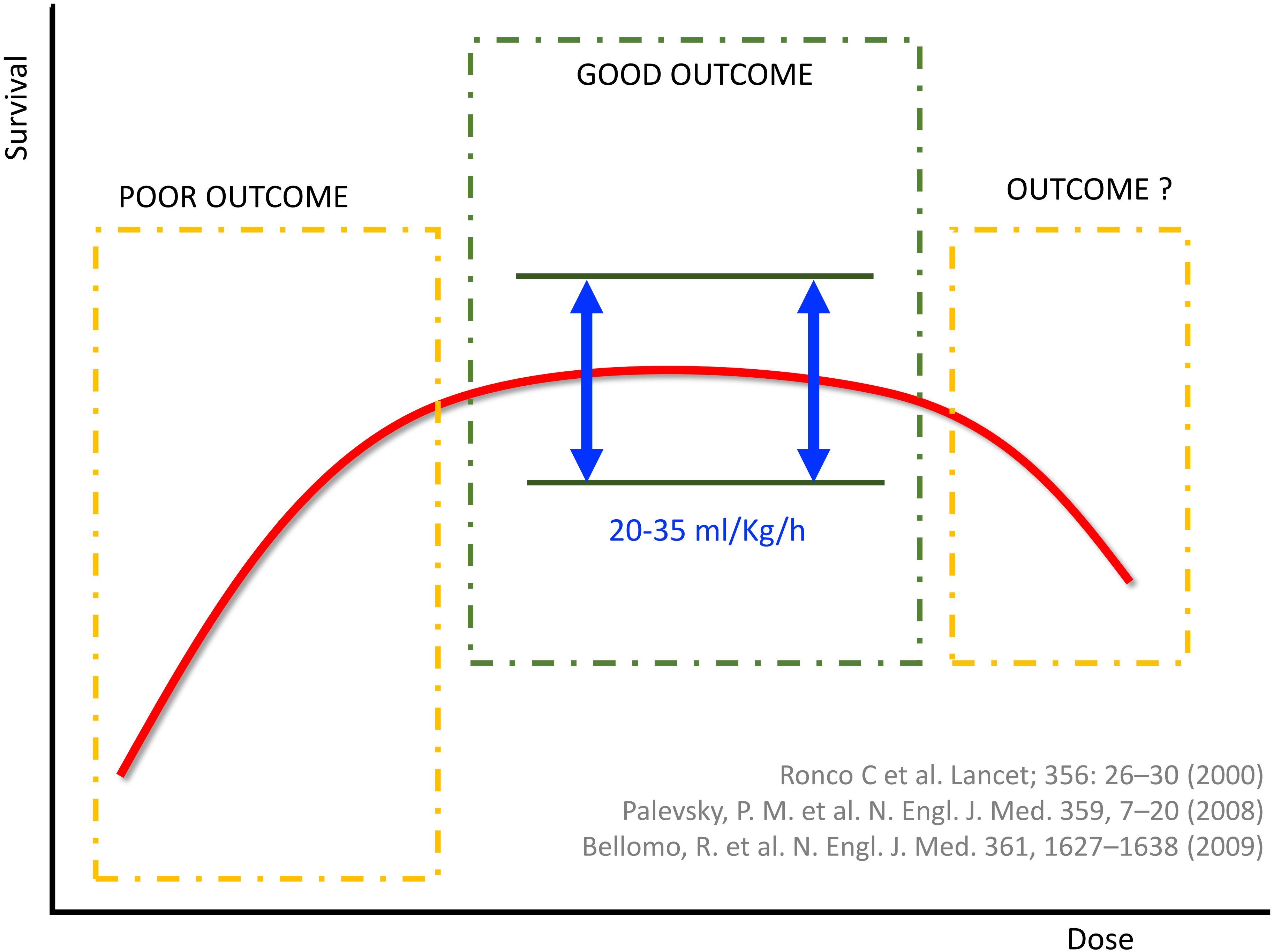
Effect of different doses in continuous veno venous hemofiltration on outcomes of acute renal failure.

Ronco C et al. Lancet 2000; 356: 26–30.

- Two large multicenter, randomized, controlled clinical trials did not find any benefit of an intensive dialysis dose over a standard dose.

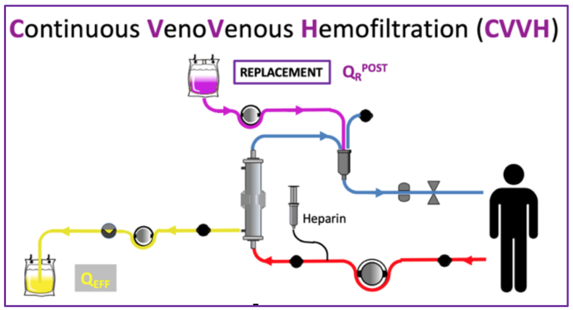
Palevsky, P. M. et al. N. Engl. J. Med. 359, 7–20 (2008).
Bellomo, R. et al. N. Engl. J. Med. 361, 1627–1638 (2009).

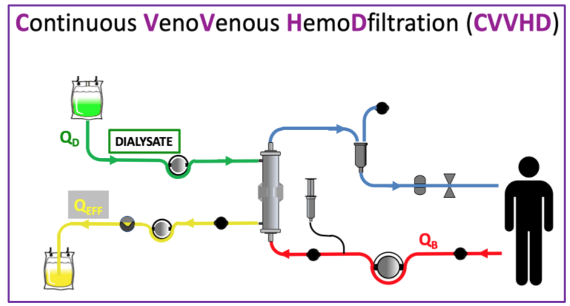
Macedo, E. et al. Nat. Rev. Nephrol. 8, 57–60 (2012)

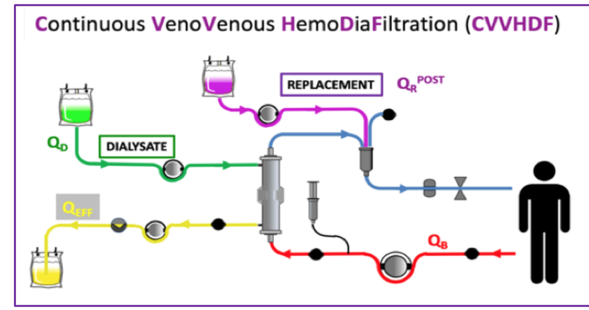

Survival
POOR OUTCOME
GOOD OUTCOME
OUTCOME ?
20-35 ml/Kg/h
Ronco C et al. Lancet; 356: 26–30 (2000)
Palevsky, P. M. et al. N. Engl. J. Med. 359, 7–20 (2008)
Bellomo, R. et al. N. Engl. J. Med. 361, 1627–1638 (2009)
Dose

The «traditional thinking» about CRRT dosing…

- **Clearance = total effluent flow (Qeff) = delivered dose = prescribed dose** → ml/Kg/h







CVVH

Prescribed dose = $Q_R^{POST} + UF^{NET}$

CVVHD

Prescribed dose = $Q_D + UF^{NET}$

CVVHDF

Prescribed dose = $Q_R^{POST} + UF^{NET} + Q_D$

} Q_{EFF}

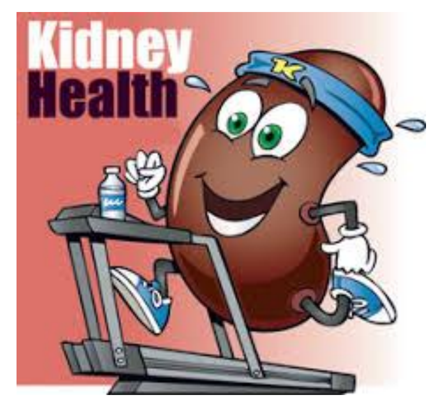
Macedo, E. et al. Nat. Rev. Nephrol. 8, 57–60 (2012)

2012

Chapter 5.8: Dose of renal replacement therapy in AKI

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*)

KIDNEY DISEASE IMPROVING GLOBAL OUTCOMES KDIGO®



“every day” clinical practice:

- 70 Kg
- **Abdominal septic shock** (anastomotic leakage) → surgery
- **Anuria**
- **Fluid Overload**

Prescribed dose:
32 ml/Kg/h

Q_R^{PRE}: 1250 ml/h

Q_R^{POST}: 1200 ml/h

UF^{NET}: 100 ml/h

Q_{EFF}: **2550** ml/h

nature REVIEWS NEPHROLOGY

PERSPECTIVES

OPINION

Effluent volume and dialysis dose in CRRT: time for reappraisal

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

Macedo, E. et al. Nat. Rev. Nephrol. 8, 57–60 (2012)

nature REVIEWS NEPHROLOGY

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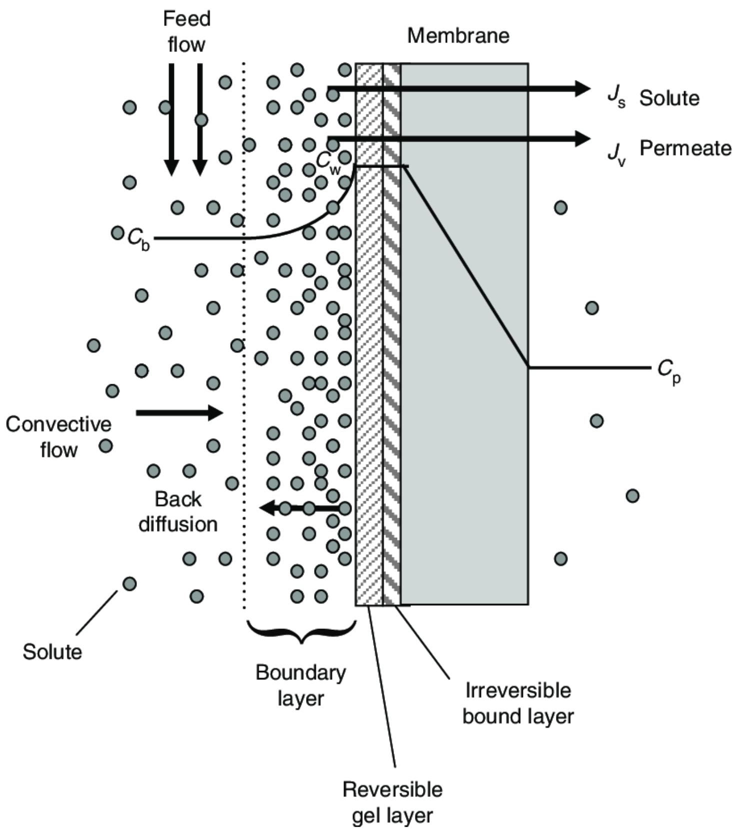
4 important factors challenge the traditional paradigm dose = effluent in patients receiving CRRT.

Macedo, E. et al. Nat. Rev. Nephrol. 8, 57–60 (2012) - *Modified*

1

- **Concentration polarization** resulting from an increased concentration of rejected solvents on the membrane surface as a function of transmembrane flow, and **protein fouling** owing to the adsorption or deposition of matter on and in the separation layer of the membrane, lead to a concentrated layer immediately adjacent to the membrane and a **decrease in diffusive transport**.



Membrane clogging

↓

- Process leading to membrane pores' saturation.
- Clogging is linked to the slow and continuous deposition of proteins and red cells debris during therapy.

↓

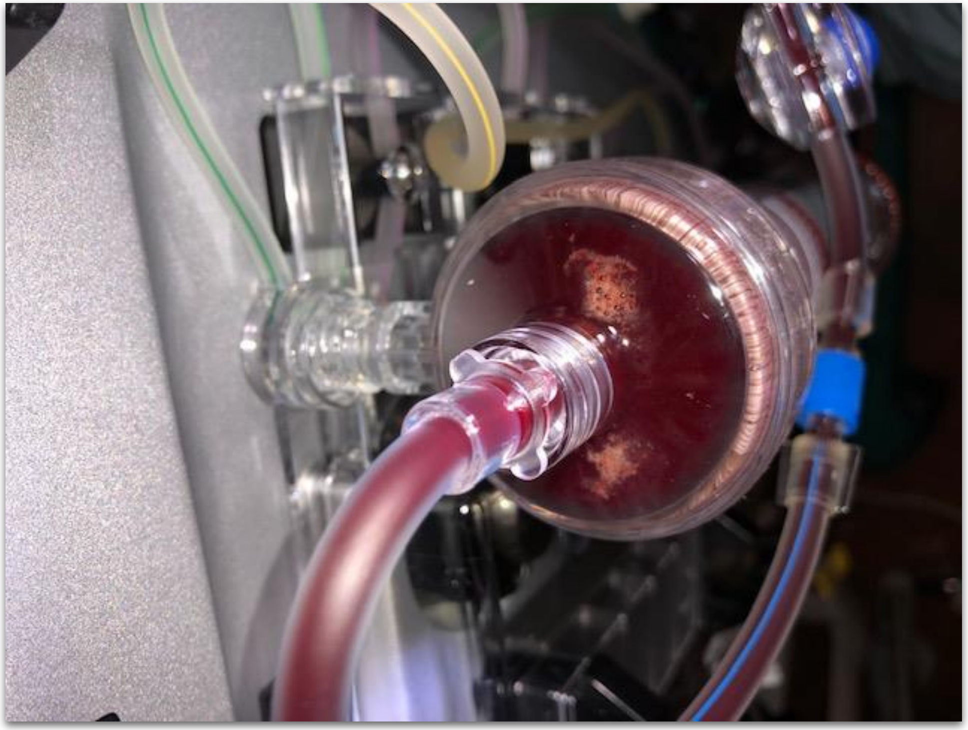
- Clogging leads to decreased membrane permeability and decreased larger molecules' sieving coefficients

Michel T et al. Curr Opin Crit Care. 2018;24:455-462

Macedo, E. et al. Nat. Rev. Nephrol. 8, 57–60 (2012)

2

- **Filter clotting** progressively causes a decline in the sieving coefficient of the membrane and reduces filter permeability. The measurement of effluent volume is driven by the settings on the CRRT machine pump and does not reflect changes in filter permeability.



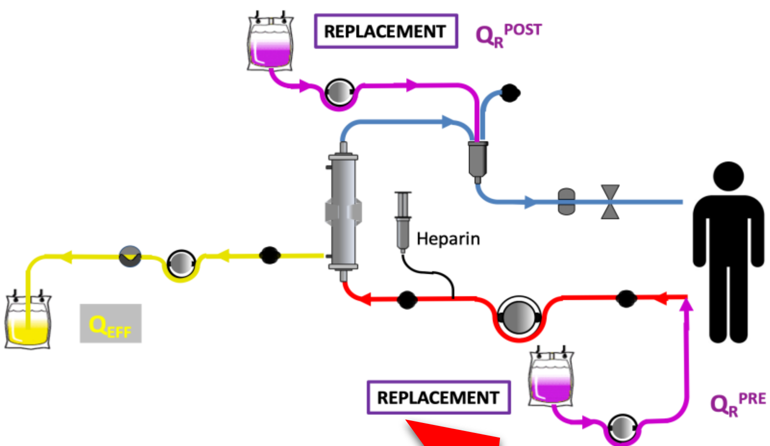
Macedo, E. et al. Nat. Rev. Nephrol. 8, 57–60 (2012)

3

• Predilution

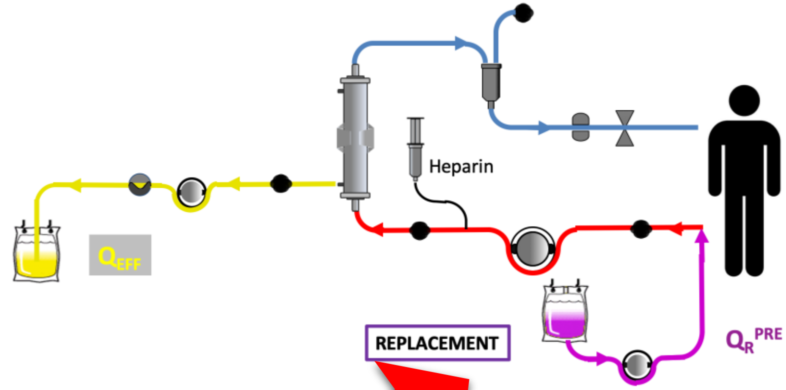
Continuous VenoVenous Hemofiltration (CVVH)

- Pre-Post-dilution
- Heparin anticoagulation



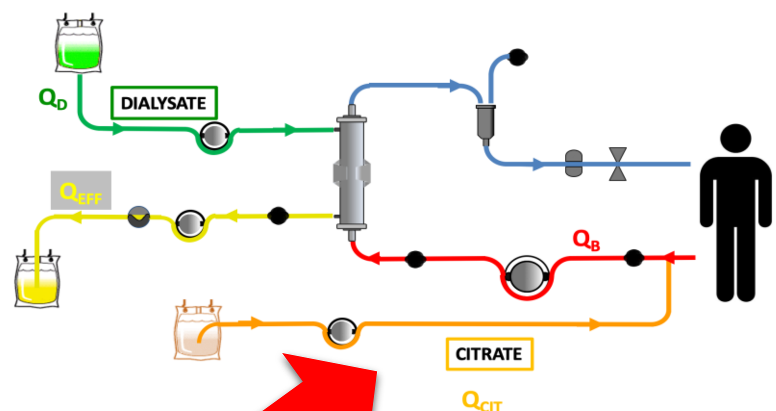
Continuous VenoVenous Hemofiltration (CVVH)

- Pre-dilution (100%)
- Heparin anticoagulation



Continuous VenoVenous HemoDialysis (CVVHD)

- Citrate anticoagulation



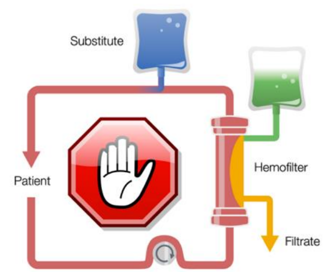
Macedo, E. et al. Nat. Rev. Nephrol. 8, 57–60 (2012)

4

- **Duration of treatments (t) vs interruptions (down time)**

“down time”



Venkataraman R et al. Journal of Critical Care, 2002:246-250

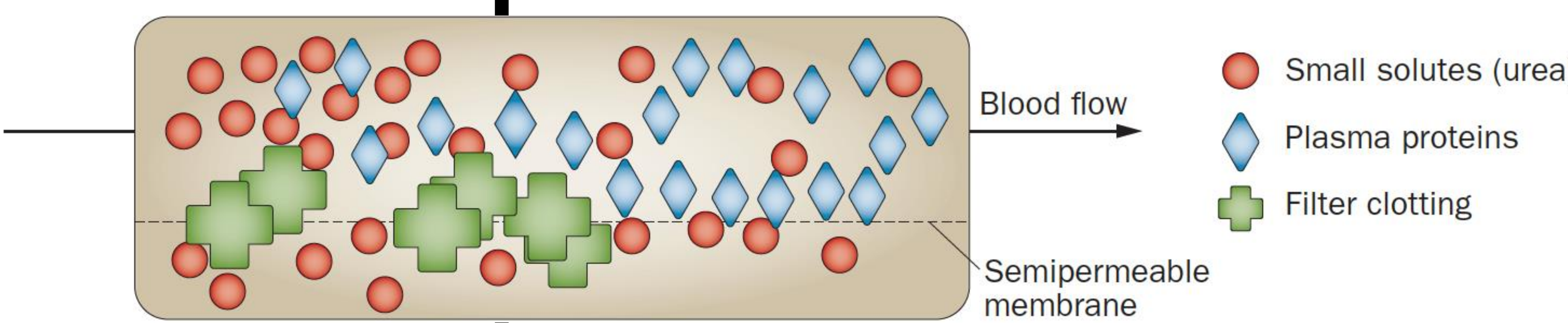
CVVH

Prescribed dose = $(Q_R^{POST} + UF^{NET}) * S$

CVVHDF

Prescribed dose = $(Q_R^{POST} + UF^{NET} + Q_D) * S$

Concentration polarization
Protein fouling
Membrane clogging
Membrane clotting



S = FUN/BUN ratio

Effluent flow ≠ clearance

Macedo, E. et al. Nat. Rev. Nephrol. 8, 57–60 (2012)

CURRENT OPINION

Continuous renal replacement therapy: understanding circuit hemodynamics to improve therapy adequacy

Thibault Michel[a], Hatem Ksouri[b], and Antoine G. Schneider[a]

STRATEGIES TO OPTIMIZE FILTER LIFE (… and FILTER EFFICIENCY)

- **Pharmacological → ANTICOAGULATION**
- **Optimizing vascular access**
- **Optimizing filtration fraction** → FF(%)=Quf/Qplasma + Qpre
- **Pre- versus post-dilution substitution fluids**

↓

Longer survival of the circuit with predilution → at the obvious <u>cost of a decrease in clearance</u>

Not an issue in purely diffusive modalities (**CVVHD**) where <u>ultrafiltration is limited to net removal</u>

- **Responses to alarms**
- **Planned filter substitution**

Michel T et al. Curr Opin Crit Care. 2018;24:455-462

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Predilution ?

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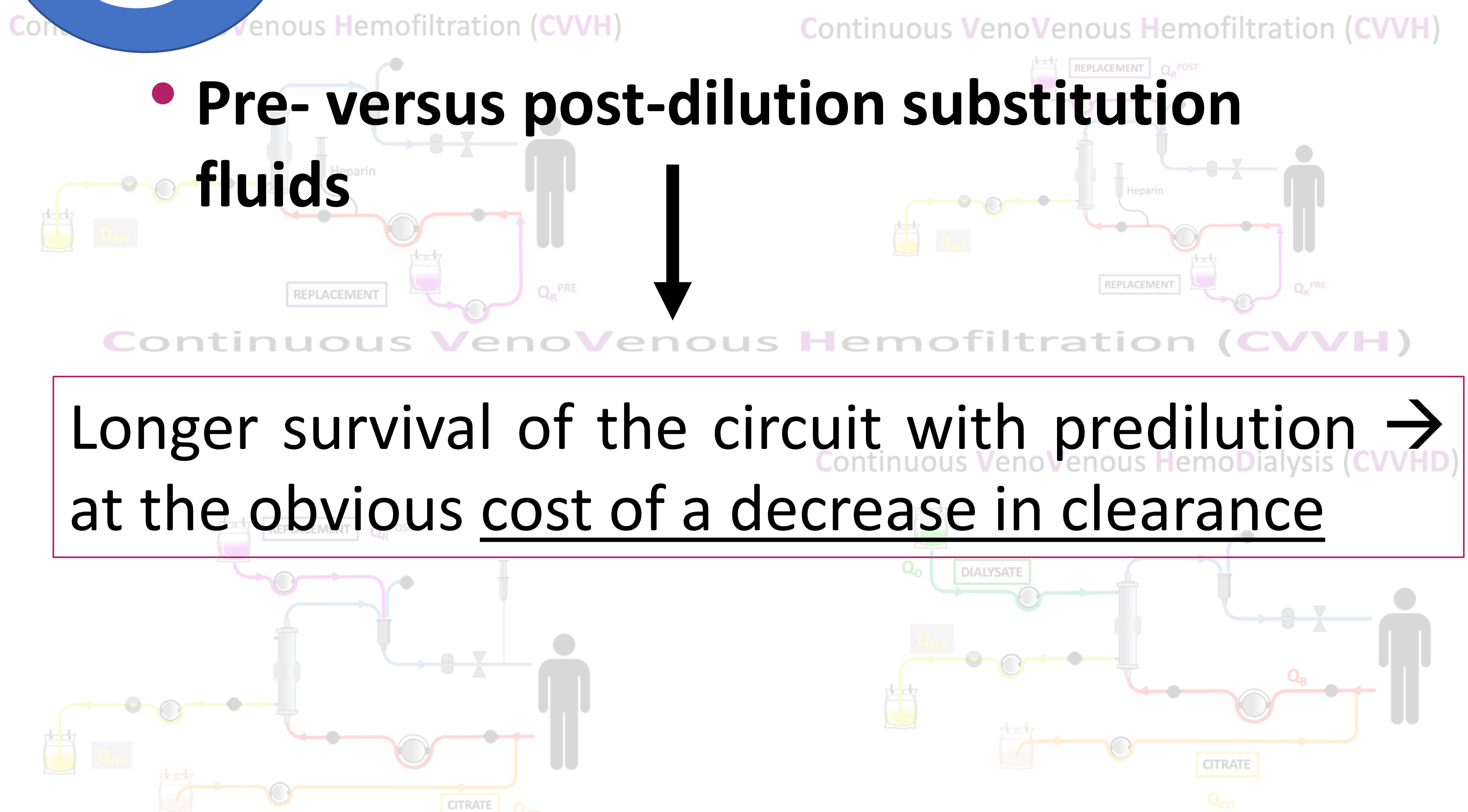


Michel T et al. Curr Opin Crit Care. 2018;24:455-462

In the ATN study, in **which predilution was used**, the combination of blood and replacement fluid flow rates suggest a dose reduction of approximately 15% in the intensive-dose group and approximately 9% in the less-intensive dose group.

Ronco, C. et al. Dialysis dose in acute kidney injury: no time for therapeutic nihilism—a critical appraisal of the Acute Renal Failure Trial Network study. Crit. Care 12, 308 (2008).

After correcting for predilution, the mean doses **of 35.3 ml/kg/h** and **22 ml/kg/h** for the intensive and less-intensive dose groups would be approximately **27 ml/kg/h** and **19 ml/kg/h**, respectively

Macedo, E. et al. Nat. Rev. Nephrol. 8, 57–60 (2012)

"every day" clinical practice:

- 70 Kg
- **Abdominal septic shock** (anastomotic leakage) → surgery
- **Anuria**
- **Fluid Overload**

Prescribed dose:
~~32 ml/Kg/h~~
18 ml/kg/h !!!

~~Q_R^{PRE}: 1250 ml/h~~

Q_R^{POST}: 1200 ml/h

UF^{NET}: 100 ml/h

Q_{EFF}: ~~2550 ml/h~~
1300 ml/h !!!

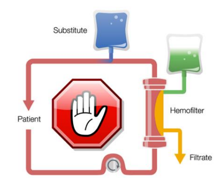
4

DOWN TIME

t = Duration of treatment

INTERRUPTION OF TREATMENT

"down time"



Venkataraman R et al. Journal of Critical Care, 2002:246-250

- ✓ ***Pump's stop***
- ✓ ***Fluid Balance alarms***
- ✓ ***Syringe changes***
- ✓ ***Patient's mobilization***
- ✓ ***Bag's change anytime***
- ✓ ***Stop for diagnostics***
- ✓ ***Stop for surgical / interventional procedures***

DOWN-TIME REDUCES PRESCRIPTION DELIVERY

Continuous renal replacement therapy: understanding circuit hemodynamics to improve therapy adequacy

Thibault Michel[a], Hatem Ksouri[b], and Antoine G. Schneider[a]

Inflow pressure

Inflow pressure is measured between the catheter and the blood pump. Because blood is actively aspirated, such pressures are typically negative, ranging between –50 and –200 mmHg. Inflow pressure is an indirect indicator of the quality and function of the vascular access. Acute drops in inflow pressure may be encountered during patient's mobilization, coughing or other instances, particularly when the vascular access is imperfectly placed. Such acute drops, even if reversible, should be prevented to optimize filter life.

Michel T et al. Curr Opin Crit Care. 2018;24:455-462

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Michel T et al. Curr Opin Crit Care. 2018;24:455-462

Current Opinion

Continuous renal replacement therapy: understanding circuit hemodynamics to improve therapy adequacy

Thibault Michel[a], Hatem Ksouri[b], and Antoine G. Schneider[a]

It is important for users to realize that **the vast majority of those** are **associated with either therapy interruption or blood pump stop**.

Delayed or inadequate response to those alarms therefore decreases therapy.

- **Responses to alarms**

Michel T et al. Curr Opin Crit Care. 2018;24:455-462

Previous studies of CRRT have shown that delivered dose is 68–89% of prescribed dose.

Evanson, J. A. et al. Am. J. Kidney Dis. 32, 731–738 (1998).
Vesconi, S. et al. Crit. Care 13, R57 (2009).

In the **RENAL** trial, the actual effluent volume computed by the machine was used to determine an estimated dialysis dose. The **difference between the prescribed dose and this estimated dose was 16% in the high-intensity dose group and 12%** in the low-intensity dose group

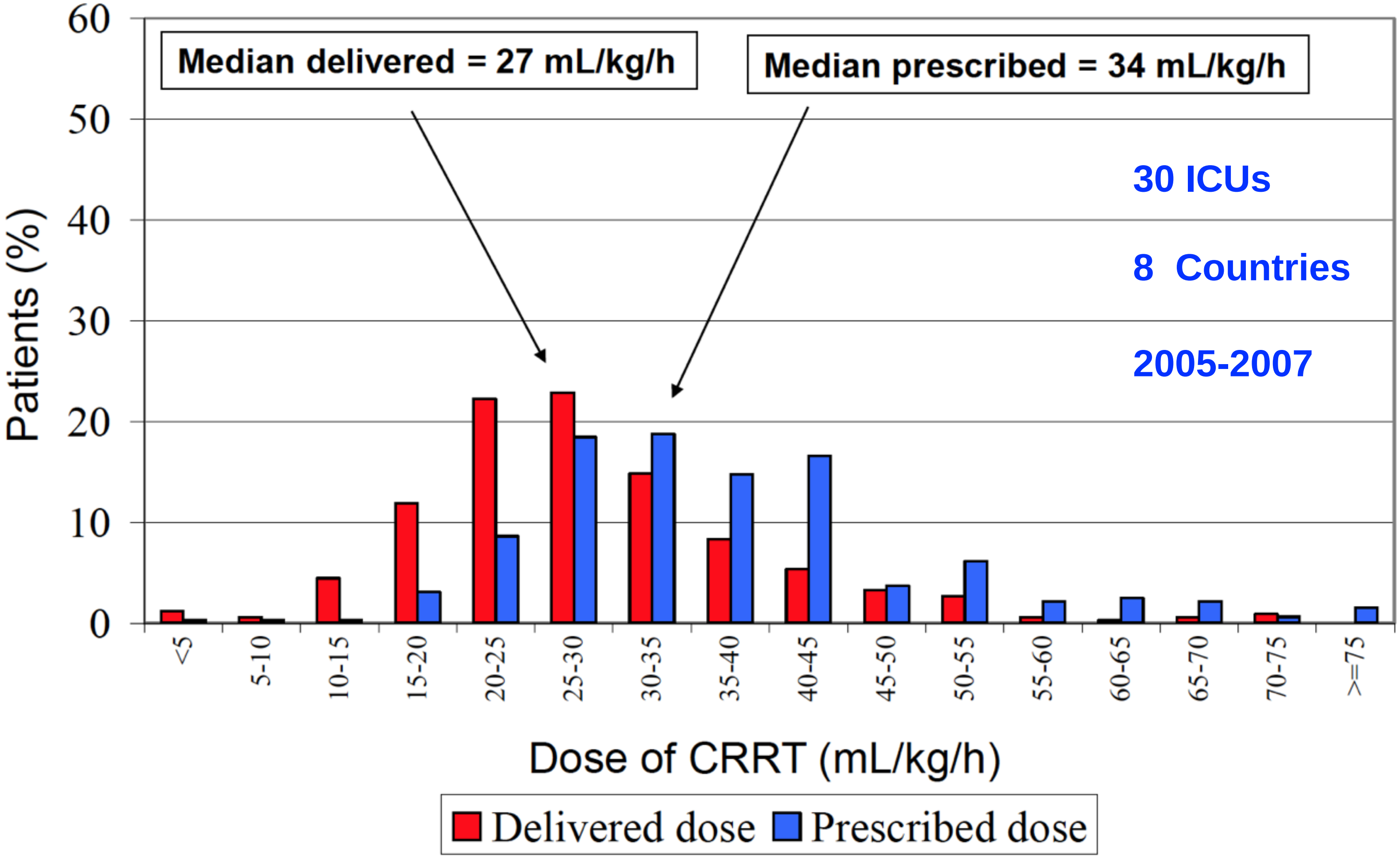
Bellomo R et al. N. Engl. J. Med. 361, 1627–1638 (2009)

In the **ATN** study, the **average daily duration of therapy was approximately 21 h** in both groups, allowing for **89% and 95% of the prescribed effluent volume** to be delivered to the intensive and less-intensive dose groups, respectively

Palewsky PM et al. N. Engl. J. Med. 359, 7–20 (2008)

Delivered dose of renal replacement therapy and mortality in critically ill patients with acute kidney injury

DoReMi Database (N=865)



Ronco C for the DOse REsponse Multicentre International collaborative Initiative (DO-RE-MI Study Group) - Critical Care 2009, 13:R57

So…how do I solve the CRRT "dose" issue..?

- Ok, I assume that clearance of my solutes equals total effluent flow… it's ok, I can't measure it, but I need to focus on catheter and anticoagulation strategies…
- GOT IT! Now I assume that total effluent flow corresponds to prescribed dose… Hum, well, yes, but track down predilution, please!
- FINE! Now that I have my "true" prescribed target, how can I be sure to actually deliver it to my patient?...

…reduce down-time: USE MODERN TECHNOLOGY!

Technological strategies to compensate for down-time

- Automatic reduction of blood flow pump in case of abrupt increases in in-flow pressures

- Automatic increases in effluent dose to gradually target a prescribed/delivered dose ratio of 1

- Automatic drain of effluent

- Prioritization of alarms

Optimizing continuous renal replacement therapy in the ICU: a team strategy

Olivier Joannes-Boyau[a], Lionel Velly[b], and Carole Ichai[c]

Curr Opin Crit Care 2018, 24:000–000

HIGH-QUALITY CRRT

- RRT "experts and champions"
- Education, simulation
- Protocols
- Data collection and evaluation
- Foster consistency
- Improve quality
- Limit variability in provision of CRRT

To recap…

- Assessing and delivering dialysis dose in patients with AKI is <u>cumbersome issue</u> in the management of critically ill patients.

- Optimizing anticoagulation (**citrate**), choosing the right catheter, managing alarms
- **Limiting the interruption** (automatic Q_B regulation)
- **Recovering the downtime**
- **Recalculating the pre-dilution impact on CRRT dose**

- Automatic adjustments of dose prescription
- Automatic data collection and analysis

THANK YOU FOR

YOUR ATTENTION!

ANY QUESTIONS?

NO? GREAT!

BYE.

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