CRRT MODALITIES

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Conflicts of Interest

Scientific partnership with the following companies:

- Baxter
- BBraun
- Biomérieux
- Estor/Toray
- Exthera
- Fresenius Medical Care
- Infomed
- Medtronic
- Nikkiso

Introduction (1): Pay attention to use correct abbreviations!

CRRT = Continuous Renal Replacement Therapy

IHD = Intermittent HemoDialysis

CVVH = Continuous Veno Venous Hemofiltration

CVVHD = Continuous Veno Venous HemoDialysis

CVVHDF = Continuous Veno Venous HemoDiaFiltration

(CRRT does not always mean CVVH!)

Introduction (2): Pay attention to not oversimplify!

HEMODIALYSIS	HEMOFILTRATION
Intermittent	Continuous
Diffusion	Convection
Small solutes	Middle molecular weight solutes

Too simplistic!

Hydraulic permeability of the membrane

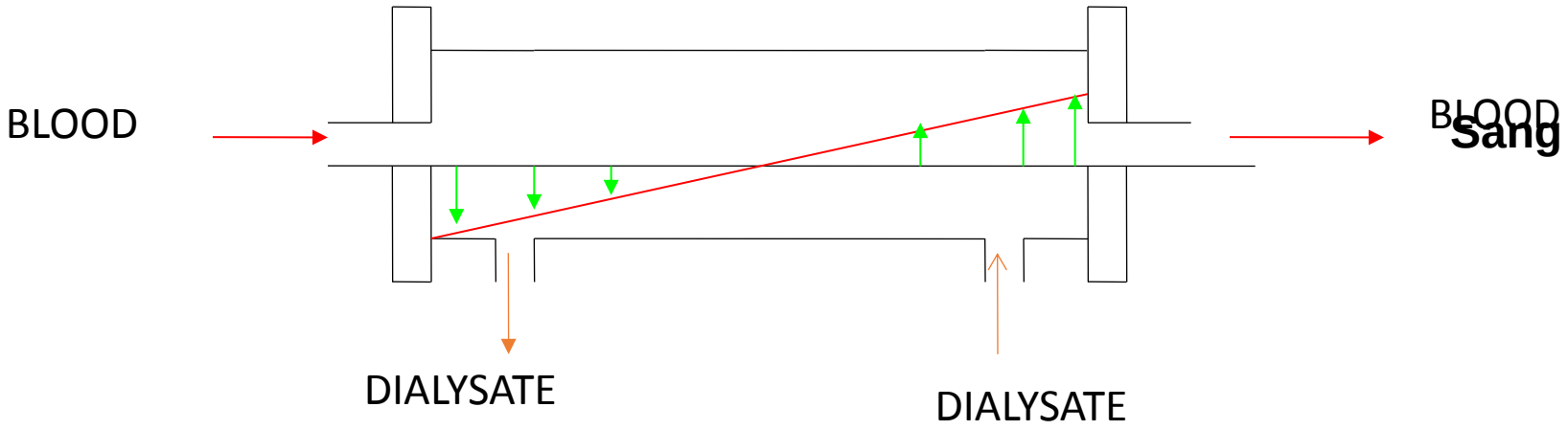
- **CVVH:** requires a RRT membrane with high hydraulic permeability (ultrafiltration coefficient K_{UF} > 20 ml/h/mmHg/m^2) in order to obtain a significant UF flow rate without an elevated TMP

$$Q_{UF} = K_{UF} \times TMP$$

- **CVVHD:** theoretically perfectly compatible with membranes with low hydraulic permeability (K_{UF} < 5 ml/h/mmHg/m^2)

if CVVHD with high-flux membrane ⟶ Internal filtration / Backfiltration

Internal filtration/backfiltration in CVVHD with high-flux filter



Internal filtration allows for additional internal convection, useful for the removal of middle molecular weight solutes

This means that modality and filter are not independent

Plus keep in mind that Internal filtration/Backfiltration is also determined by the blood flow

Blood Purif 1991;9:74–84

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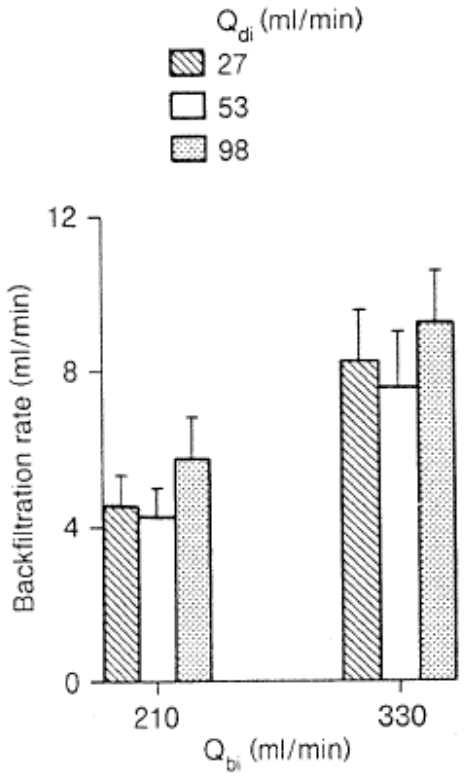
0253–5068/91/0092–0074$2.75/0

Measurement of Backfiltration Rates during Hemodialysis with Highly Permeable Membranes

John K. Leypoldt, Bärbel Schmidt, Hans J. Gurland

Nephrology Department, Klinikum Grosshadern, University of Muni



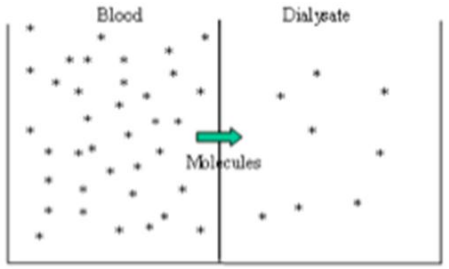
Leypoldt et al. Blood Purif 1991

In 2019:

HEMODIALYSIS	HEMOFILTRATION
Intermittent or Continuous	Continuous (or intermittent)
Diffusion +/- internal convection	Convection
Small solutes +/- middle molecules	Small and middle molecules

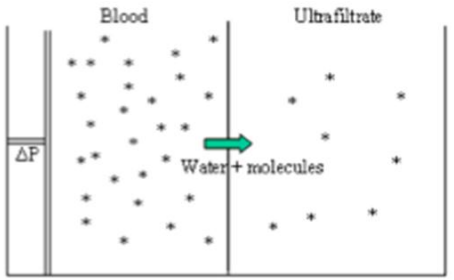
Which modality for my RRT sessions?

A DIFFUSION



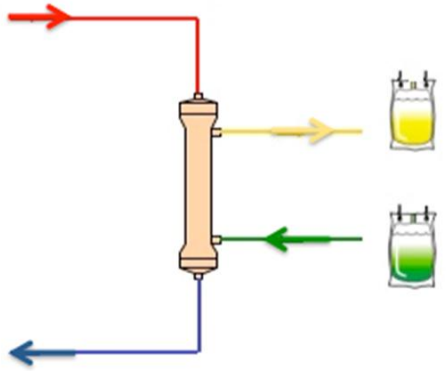
Concentration gradient

B CONVECTION

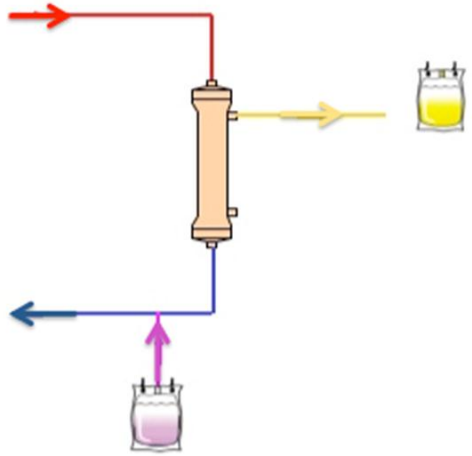


Hydrostatic pressure gradient

C HEMODIALYSIS CIRCUIT



D HEMOFILTRATION CIRCUIT



= What are my 3 goals for my RRT sessions?

What are my 3 goals for my RRT sessions?

Goals	
1) Hemodynamic stability	
2) Significant filter lifespan	
3) Optimization of the molecular clearances over time = stability of membrane performance over time	

What are my 3 goals for my RRT sessions?

Goals	IMPACTED BY RRT MODALITY?
1) Hemodynamic stability	
2) Significant filter lifespan	
3) Optimization of the molecular clearances over time = stability of membrane performance over time	

What are my 3 goals for my RRT sessions?

Goals	IMPACTED BY RRT MODALITY?
1) Hemodynamic stability	IHD versus CRRT
2) Significant filter lifespan	Anticoagulation strategy with CVVH or CVVHD
3) Optimization of the molecular clearances over time = stability of membrane performance over time	CVVH versus CVVHD

What are my 3 goals for my RRT sessions?

Goals	IMPACTED BY RRT MODALITY?
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IHD vs CRRT: a 20-yr controversy

IHD

CRRT

Advantages of IHD

- Avoids risks associated with continuous anticoagulation
- (Easily deployed at the bedside)
- Allows the patient to achieve greater mobility
- Cheaper "*per se*"

Advantages of CRRT

- Greater hemodynamic stability
- Continuous control of volume status
- Steady control of electrolyte and acid-base status
- Temperature control
- Avoidance of solute swings and cerebral edema
- Superior uremic control

RRT modality (IHD vs CRRT)

5.4.6: We suggest not using antibiotic locks for prevention of catheter-related infections of nontunneled dialysis catheters in AKI requiring RRT. (*2C*)

5.5.1: We suggest to use dialyzers with a biocompatible membrane for IHD and CRRT in patients with AKI. (*2C*)

5.6.1: Use continuous and intermittent RRT as complementary therapies in AKI patients. (*Not Graded*)

5.6.2: We suggest using CRRT, rather than standard intermittent RRT, for hemodynamically unstable patients. (*2B*)

5.6.3: We suggest using CRRT, rather than intermittent RRT, for AKI patients with acute brain injury or other causes of increased intracranial pressure or generalized brain edema. (*2B*)

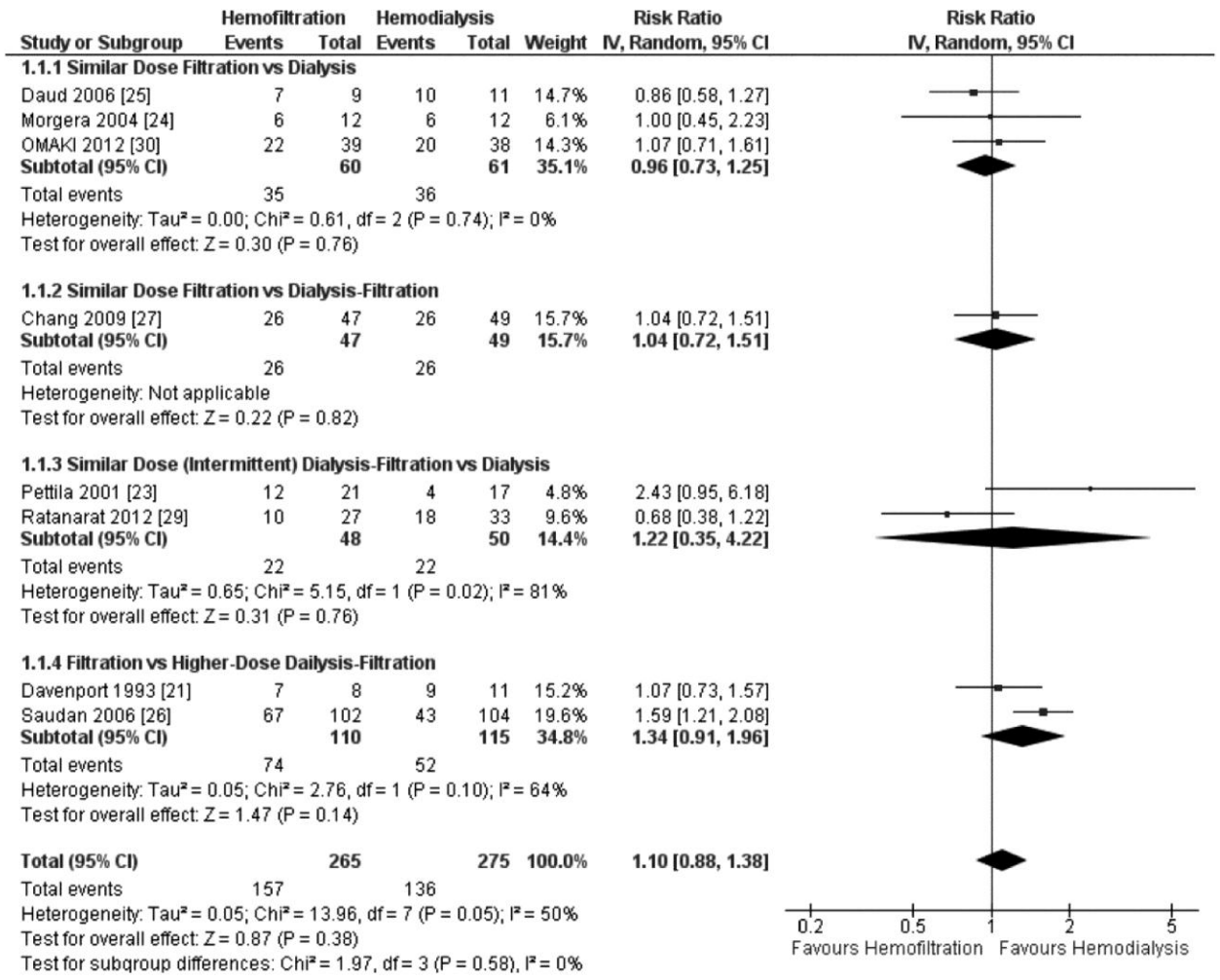
5.7.1: We suggest using bicarbonate, rather than lactate, as a buffer in dialysate and replacement fluid for RRT in patients with AKI. (*2C*)

5.7.2: We recommend using bicarbonate, rather than lactate, as a buffer in dialysate and replacement fluid for RRT in patients with AKI and circulatory shock. (*1B*)

5.7.3: We suggest using bicarbonate, rather than lactate, as a buffer in dialysate and replacement fluid for RRT in

KDIGO guidelines. Kidney Int suppl 2012

CRRT vs IHD and mortality



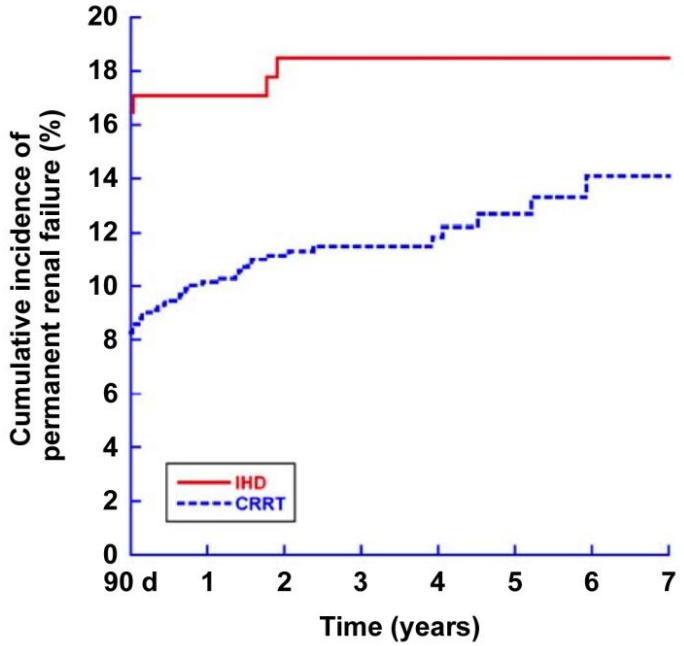
Friedrich et al. Crit Care 2012

Max Bell
SWING
Fredrik Granath
Staffan Schön
Anders Ekbom
Claes-Roland Martling

Continuous renal replacement therapy is associated with less chronic renal failure than intermittent haemodialysis after acute renal failure

Intensive Care Med (2007) 33:773–780

Renal failure among patients surviving 90 days:



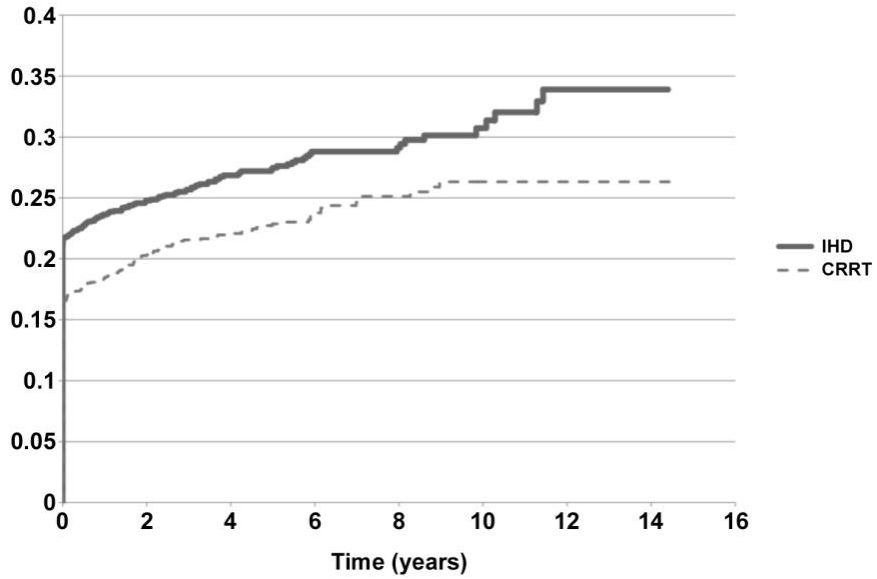
	CRRT ($n = 944$)		IHD ($n = 158$)			
	n (%)	OR	n (%)	OR[a] (95% CI)	OR[b] (95% CI)	OR[c] (95% CI)
ESRD	78 (8.3)	1.0	26 (16.5)	2.19 (1.4–3.5)	2.13 (1.3–3.5)	2.60 (1.5–4.3)

[a] OR, crude
[b] OR, adjusted for age, sex, diabetes or heart failure before admission and calendar year
[c] OR, adjusted for age, sex, diabetes or heart failure before admission, calendar year, hospital type and main diagnosis at ICU

Bell et al. Intensive Care Med 2007

The Association Between Renal Replacement Therapy Modality and Long-Term Outcomes Among Critically Ill Adults With Acute Kidney Injury: A Retrospective Cohort Study

Cumulative risk of chronic dialysis among critically ill patients with AKI surviving to 90 days after commencement of RRT who were initially treated with CRRT vs IHD:



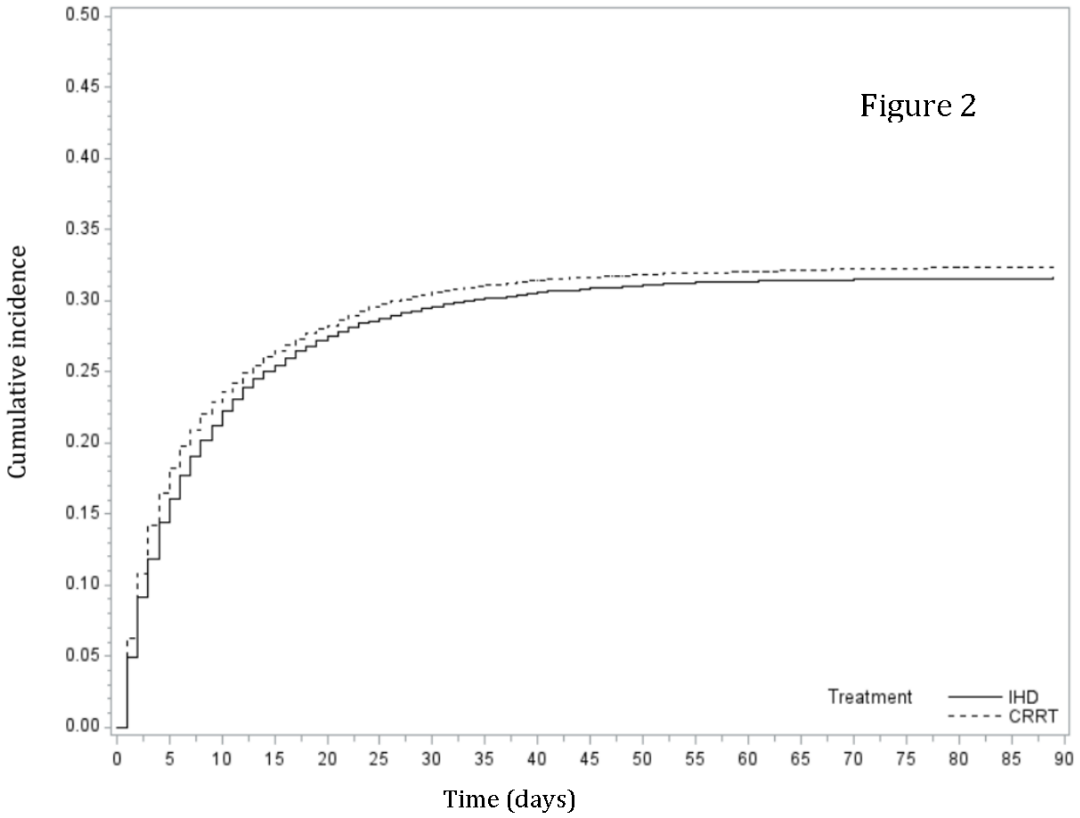
Outcomes for patients with AKI surviving to 90 days, initiated on CRRT vs IHD:

Outcome	CRRT ($n = 2,004$)		IHD ($n = 2,004$)		Hazard Ratio (95% CI) for CRRT vs IHD	p
	n (%)	Incidence Rate per 100 Person-Years	*n* (%)	Incidence Rate per 100 Person-Years		
Chronic dialysis	435 (22)	6.5	533 (27)	8.2	0.75 (0.65–0.87)	< 0.0001
Death	883 (44)	11.2	905 (45)	11.4	1.02 (0.91–1.14)	0.73

Wald R et al. Crit Care Med 2014

Multivariate analysis:
1 million ICU patients over 4 years

Variable	Odds ratio (95% CI)	*p*
Technique (IHD vs CRRT)	**0.912 (0.835–0.996)**	**0.04**
Shock (yes vs no)	1.188 (1.060–1.331)	0.003
Vasopressors (yes vs no)	1.192 (1.088–1.305)	0.0002
Ventilation (yes vs no)	1.541 (1.404–1.692)	<0.0001
Cardiac arrest (yes vs no)	1.243 (1.009–1.531)	0.0413
Cardiac surgery	1.676 (1.281–2.192)	0.0002
Non terminal CKD (yes vs no)	0.635 (0.575–0.702)	<0.0001
Center (<250 vs >450 beds)	0.547 (0.427–0.702)	<0.0001



Bonnassieux et al. Crit Care Med 2017

What are my 3 goals for my RRT sessions?

Goals	IMPACTED BY RRT MODALITY?
1) Hemodynamic stability	IHD versus CRRT
2) Significant filter lifespan	Anticoagulation strategy with CVVH or CVVHD
3) Optimization of the molecular clearances over time = stability of membrane performance over time	CVVH versus CVVHD

Schilder et al. Critical Care 2014, 18:472
http://ccforum.com/content/18/4/472

CRITICAL CARE

RESEARCH Open Access

Citrate anticoagulation versus systemic heparinisation in continuous venovenous hemofiltration in critically ill patients with acute kidney injury: a multi-center randomized clinical trial

Louise Schilder[1*], S Azam Nurmohamed[1], Frank H Bosch[2], Ilse M Purmer[3], Sylvia S den Boer[4], Cynthia G Kleppe[5], Marc G Vervloet[1], Albertus Beishuizen[6], Armand RJ Girbes[6], Pieter M ter Wee[1], AB Johan Groeneveld[7] and for the CASH study group

Stucker et al. Critical Care (2015) 19:91
DOI 10.1186/s13054-015-0822-z

CRITICAL CARE

RESEARCH Open Access

Efficacy and safety of citrate-based anticoagulation compared to heparin in patients with acute kidney injury requiring continuous renal replacement therapy: a randomized controlled trial

Fabien Stucker[1†], Belen Ponte[1†], James Tataw[1], Pierre-Yves Martin[1], Hannah Wozniak[2], Jérome Pugin[2] and Patrick Saudan[1*]

A Randomized Controlled Trial of Regional Citrate Versus Regional Heparin Anticoagulation for Continuous Renal Replacement Therapy in Critically Ill Adults*

David J. Gattas, MD, MMed (ClinEpi), FCICM, FRACP[1,2];
Dorrilyn Rajbhandari, RN Post Grad Dip (Clinical Nursing)[1,2]; Celia Bradford, MD, FCICM[3];
Heidi Buhr, RN, MClinTPrac[1]; Serigne Lo, PhD, AStat[2];
Rinaldo Bellomo, MBBS, MD (Hons), FRACP, FCICM, PG Dip Echo[4,5]

Citrate =

- Less bleeding complications
- Higher filter life time
- Less unwanted stops = optimized administered dialysis dose

Schilder et al. Critical Care 2014
Stucker et al. Critical Care 2015
Gattas et al. Crit Care Med 2015

Anticoagulation and KDIGO guidelines

Chapter 5.3: Anticoagulation

5.3.2.2: For anticoagulation in CRRT, we suggest using regional citrate anticoagulation rather than heparin in patients who do not have contraindications for citrate. *(2B)*

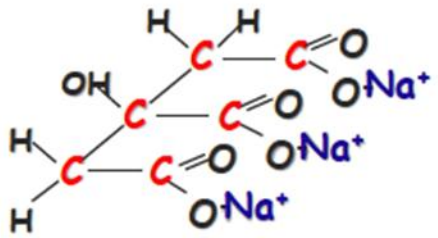
5.3.2.3: For anticoagulation during CRRT in patients who have contraindications for citrate, we suggest using either unfractionated or low-molecular-weight heparin, rather than other anticoagulants. *(2C)*

KDIGO guidelines. Kidney Int 2012

Any issue(s) with citrate?

Risk of metabolic complications

Trisodic Citrate (Na_3Citrate)

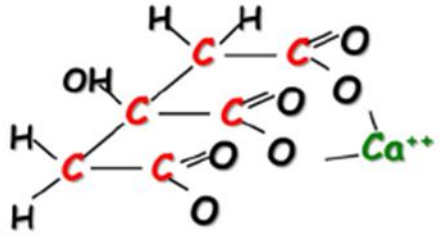


Na_3Citrate

Ca^{2+}

Na^+ +++++

Cit-Ca^{2+} Complex



CaCitrate

Strong Ion Difference

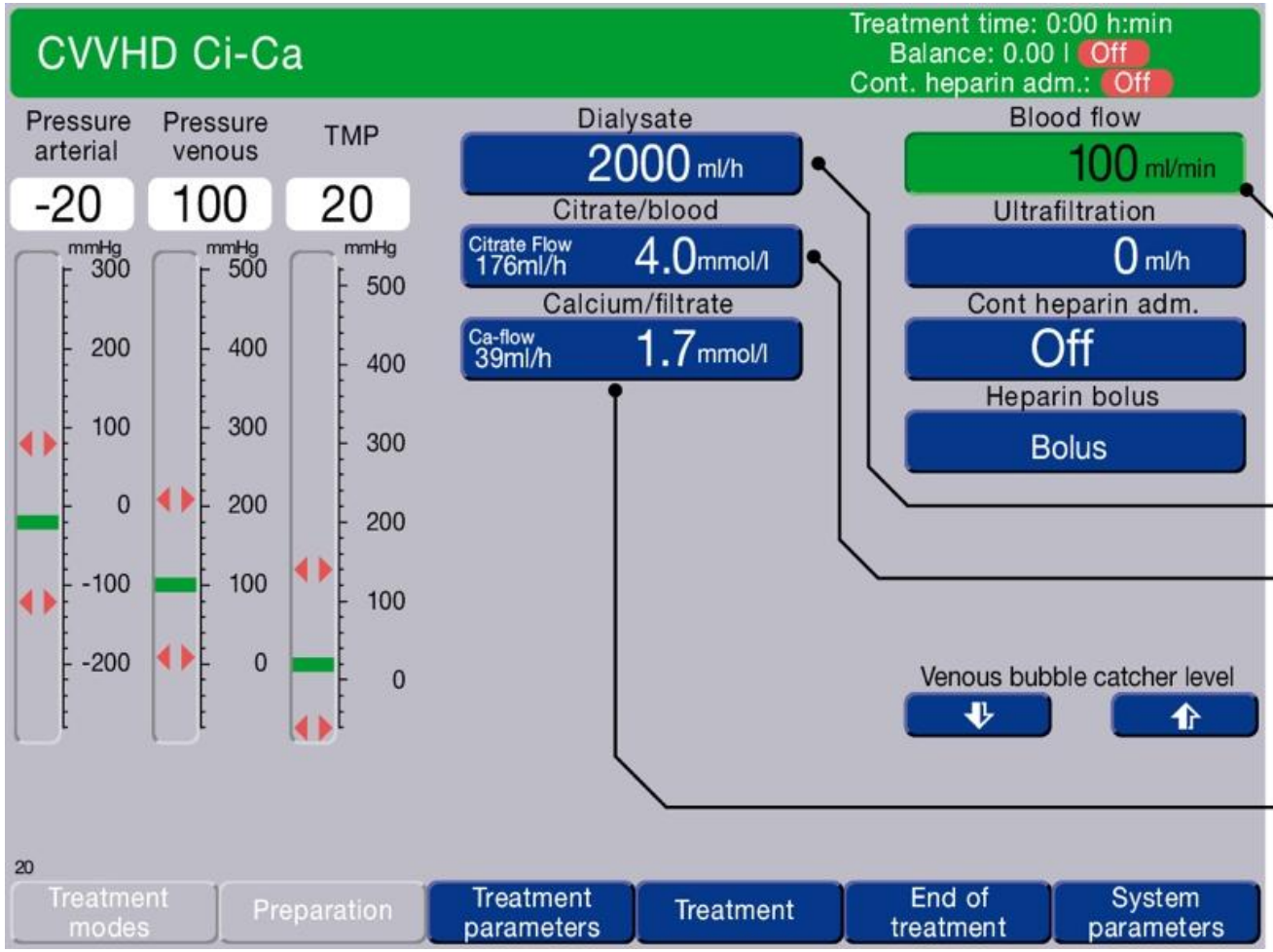
$$SID = (Na^+ + K^+ + Ca^{2+} + Mg^{2+} + UA^+) - (Cl^- + UA^-)$$

- Metabolic alkalosis
- Metabolic acidosis
- Hypernatremia
- Hypocalcemia
- Hypercalcemia
- Hypomagnesemia

What is the best way to avoid these metabolic complications?

= How should I proceed to give to the patient as little citrate as possible?

Citrate anticoagulation is now safe because pumps work together!

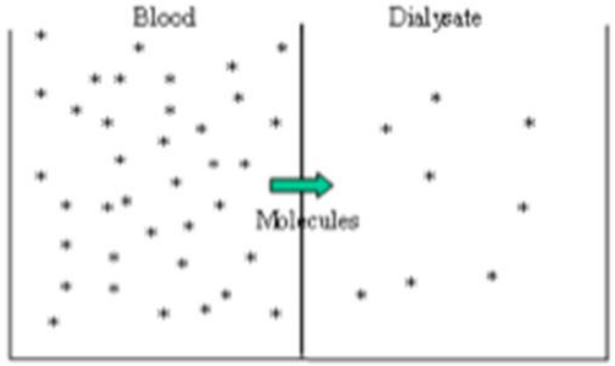


Blood pump and citrate pump work together

Effluent pump and calcium pump work together

A

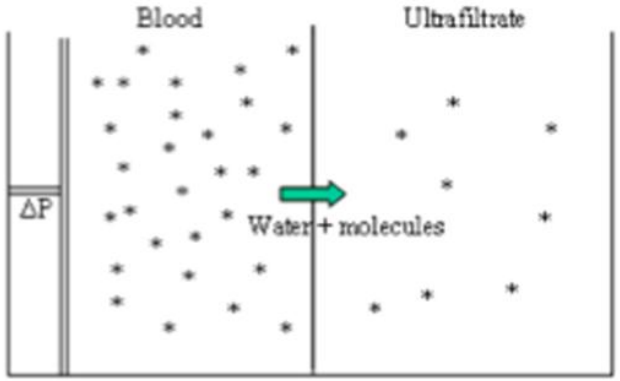
DIFFUSION



Concentration gradient

B

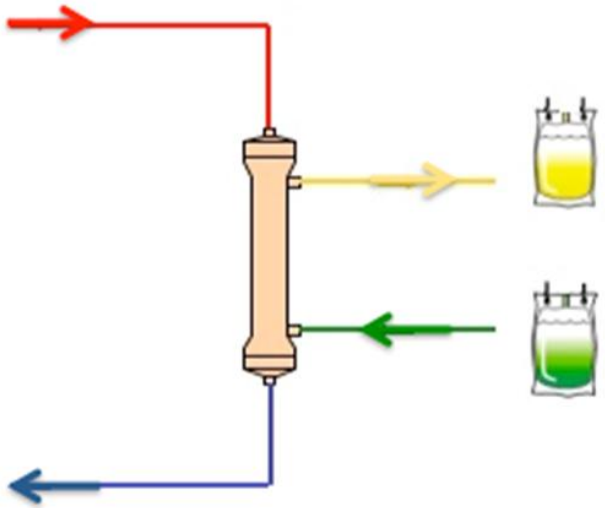
CONVECTION



Hydrostatic pressure gradient

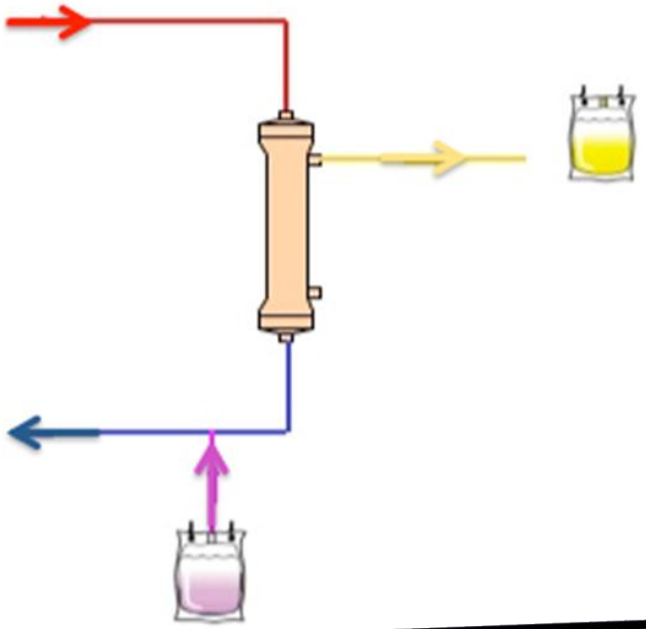
C

HEMODIALYSIS CIRCUIT

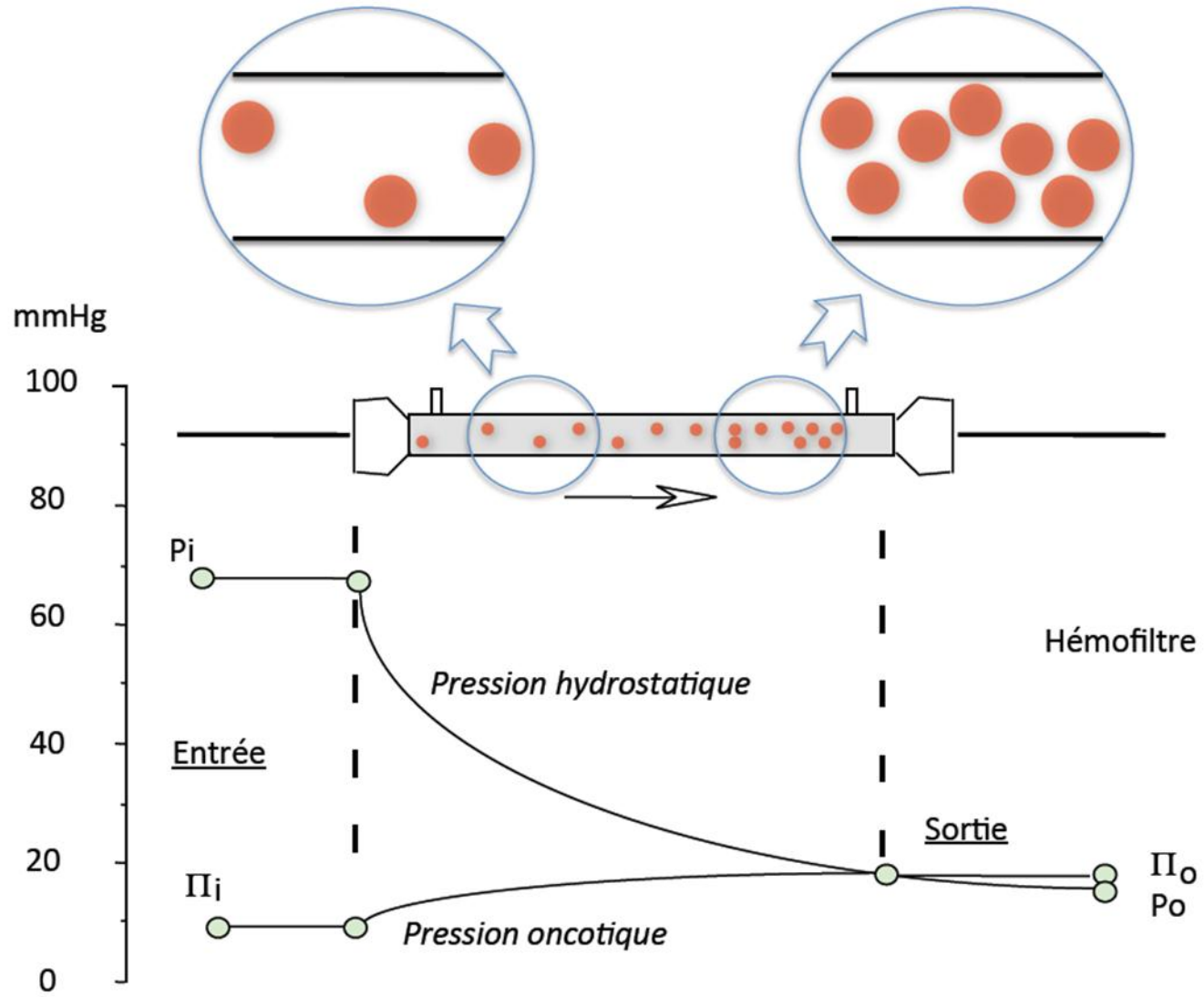


D

HEMOFILTRATION CIRCUIT



FILTRATION FRACTION



Courtesy of Pr. Didier Journois

FILTRATION FRACTION

FF = UF Flow / Blood flow (if 100 % post dilution)

FF = (Pre + Post + weigh loss) / (Blood flow + Pre)

Optimal FF = 20-25 %

Garzotto *et al. Critical Care* (2016) 20:196
DOI 10.1186/s13054-016-1355-9

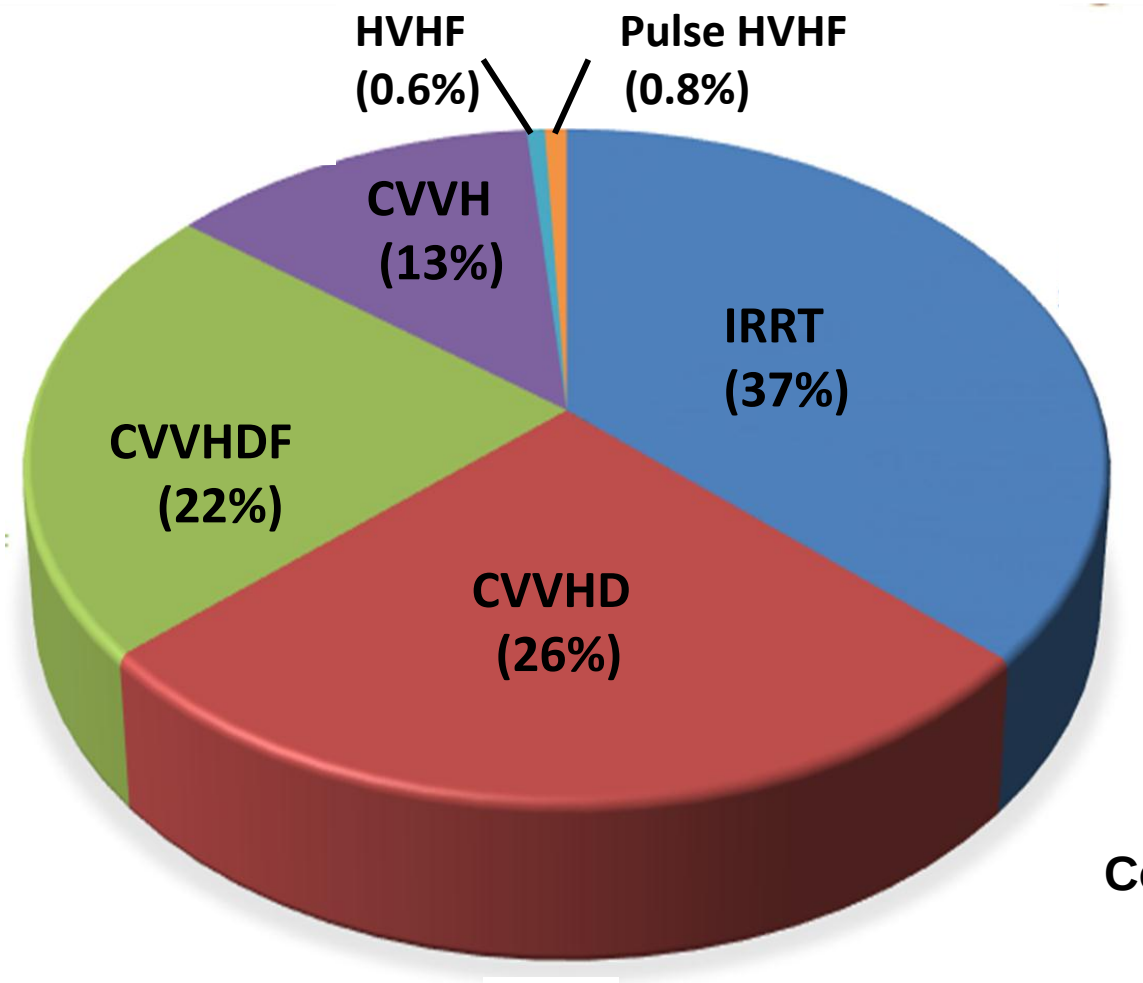
Critical Care

RESEARCH Open Access

The Dose Response Multicentre Investigation on Fluid Assessment (DoReMIFA) in critically ill patients

F. Garzotto[1,2*], M. Ostermann[3], D. Martín-Langerwerf[4], M. Sánchez-Sánchez[5], J. Teng[6], R. Robert[7], A. Marinho[8], M. E. Herrera-Gutierrez[9], H. J. Mao[10], D. Benavente[11], E. Kipnis[12], A. Lorenzin[2], D. Marcelli[13], C. Tetta[13], C. Ronco[1,2] and for the DoReMIFA study group

Modality of RRT (all sessions), DoRéMiFa study



Courtesy of Marlies Ostermann

Type of anticoagulation for CRRT (DoRéMiFa study)

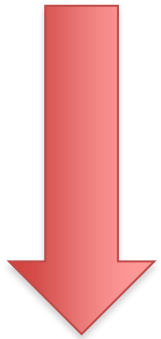
	CVVH	CVVHD	CVVHDF	Others
None	33%	11%	54%	2%
Heparin	20%	34%	42%	4%
Citrate	0%	99%	0%	1%

Courtesy of Marlies Ostermann

Citrate + CVVHD

1- Low Blood Flow = Small amount of citrate needed

2- CVVHD (Diffusion) = possibility to remove a large proportion of Ci-Ca complexes if necessary



Allow for a prudent use of citrate anticoagulation in patients in whom citrate would usually be contra-indicated (liver insufficiency, MOF, hyperlactatemia…)

Citrate + CVVHD + liver insufficiency

Schultheiß *et al. Critical Care* 2012, **16**:R162
http://ccforum.com/content/16/4/R162

CRITICAL CARE

RESEARCH Open Access

Continuous venovenous hemodialysis with regional citrate anticoagulation in patients with liver failure: a prospective observational study

Caroline Schultheiß[1*], Bernd Saugel[1], Veit Phillip[1], Philipp Thies[1], Sebastian Noe[1], Ulrich Mayr[1], Bernhard Haller[2], Henrik Einwächter[1], Roland M Schmid[1] and Wolfgang Huber[1]

Journal of Critical Care 29 (2014) 265–271

Contents lists available at ScienceDirect

Journal of Critical Care

journal homepage: www.jccjournal.org

Incidence and outcome of metabolic disarrangements consistent with citrate accumulation in critically ill patients undergoing continuous venovenous hemodialysis with regional citrate anticoagulation

Dmytro Khadzhynov, MD, Christin Schelter, Ina Lieker, MD, Alice Mika, Oliver Staeck, MD, Hans.-H. Neumayer, MD, Harm Peters, MD *, Torsten Slowinski, MD

Department of Nephrology, Charité Universitätsmedizin Berlin, Charité Campus Mitte, Humboldt University Berlin, D-10117 Berlin, Germany

Slowinski *et al. Critical Care* (2015) 19:349
DOI 10.1186/s13054-015-1066-7

CRITICAL CARE

RESEARCH Open Access

Safety and efficacy of regional citrate anticoagulation in continuous venovenous hemodialysis in the presence of liver failure: the Liver Citrate Anticoagulation Threshold (L-CAT) observational study

Torsten Slowinski[1*], Stanislao Morgera[1], Michael Joannidis[2], Thomas Henneberg[3], Reto Stocker[4], Elin Helset[5], Kirsti Andersson[6], Markus Wehner[7], Justyna Kozik-Jaromin[8], Sarah Brett[9], Julia Hasslacher[2], John F. Stover[4], Harm Peters[1], Hans-H. Neumayer[1] and Detlef Kindgen-Milles[9]

Safety and Efficacy of Citrate Anticoagulation for Continuous Renal Replacement Therapy for Acute Kidney Injury After Liver Transplantation: A Single-Center Experience

N. Pertica[a,*], L. Cicciarella[a], A. Carraro[b], U. Montin[b], P. Violi[b], A. Lupo[a], and G. Zaza[a]

[a]Renal and Dialysis Unit, University Hospital of Verona, Verona, Italy; and [b]Department of General Surgery and Dentistry, Liver Transplant Unit, University Hospital of Verona, Verona, Italy

« Feasible » ; « safely used » ; « low incidence of disarrangements »

What are my 3 goals for my RRT sessions?

Goals	IMPACTED BY RRT MODALITY?
1) Hemodynamic stability	IHD versus CRRT
2) Significant filter lifespan	Anticoagulation strategy with CVVH or CVVHD
3) Optimization of the molecular clearances over time = stability of membrane performance over time	CVVH versus CVVHD

Decrease of membrane efficacy over time

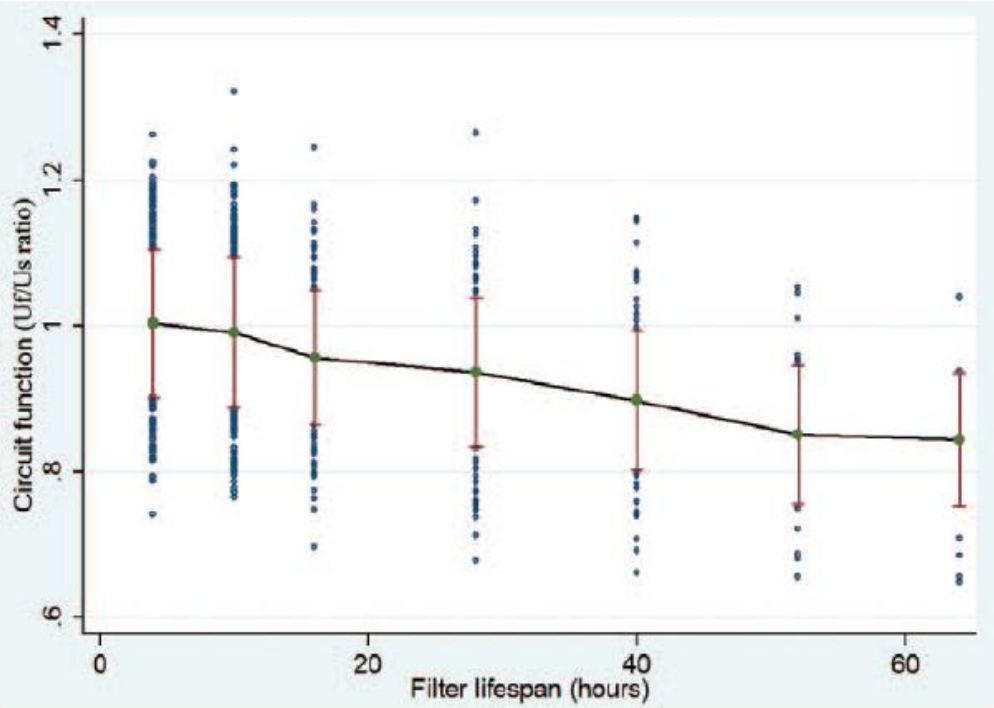


Figure 1. Filter function (**Equation 6**) declined progressively over time. U_f refers to urea measured in ultrafiltrate, and U_s refers to urea measured in the blood.

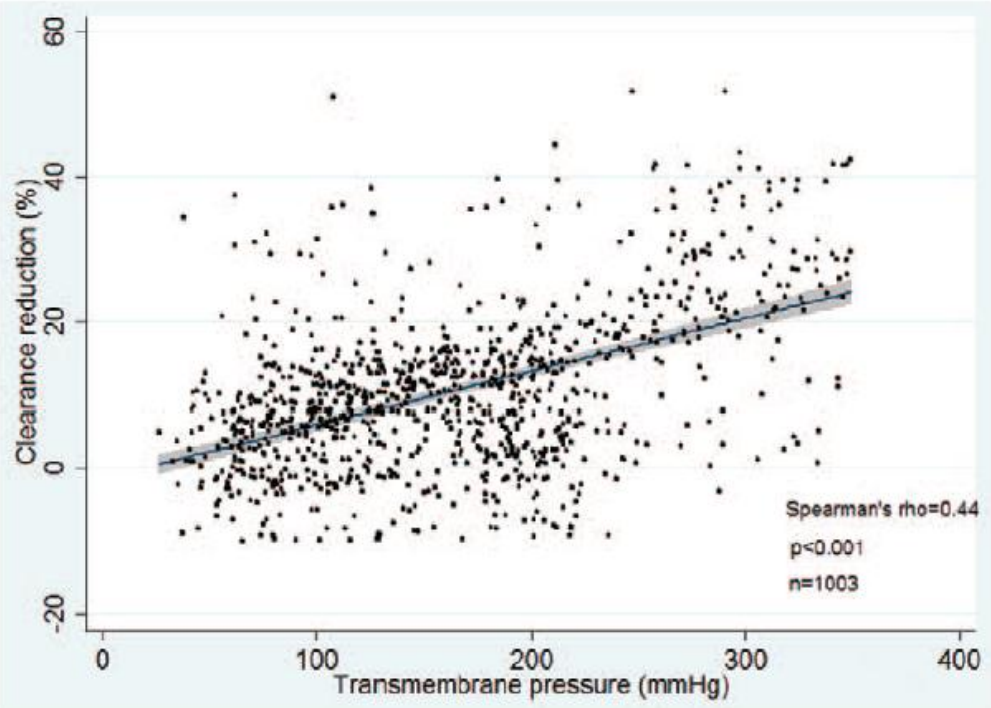
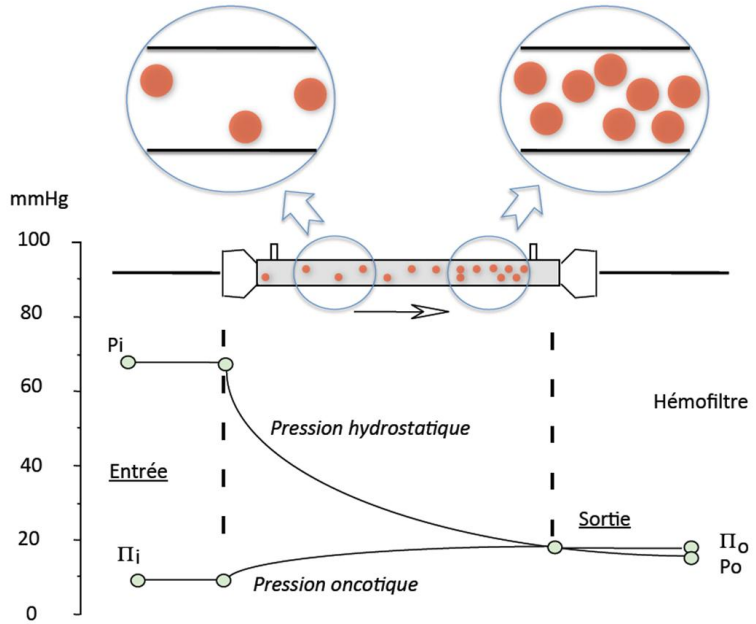
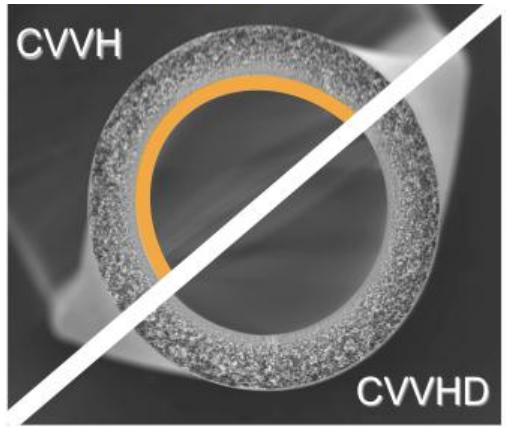


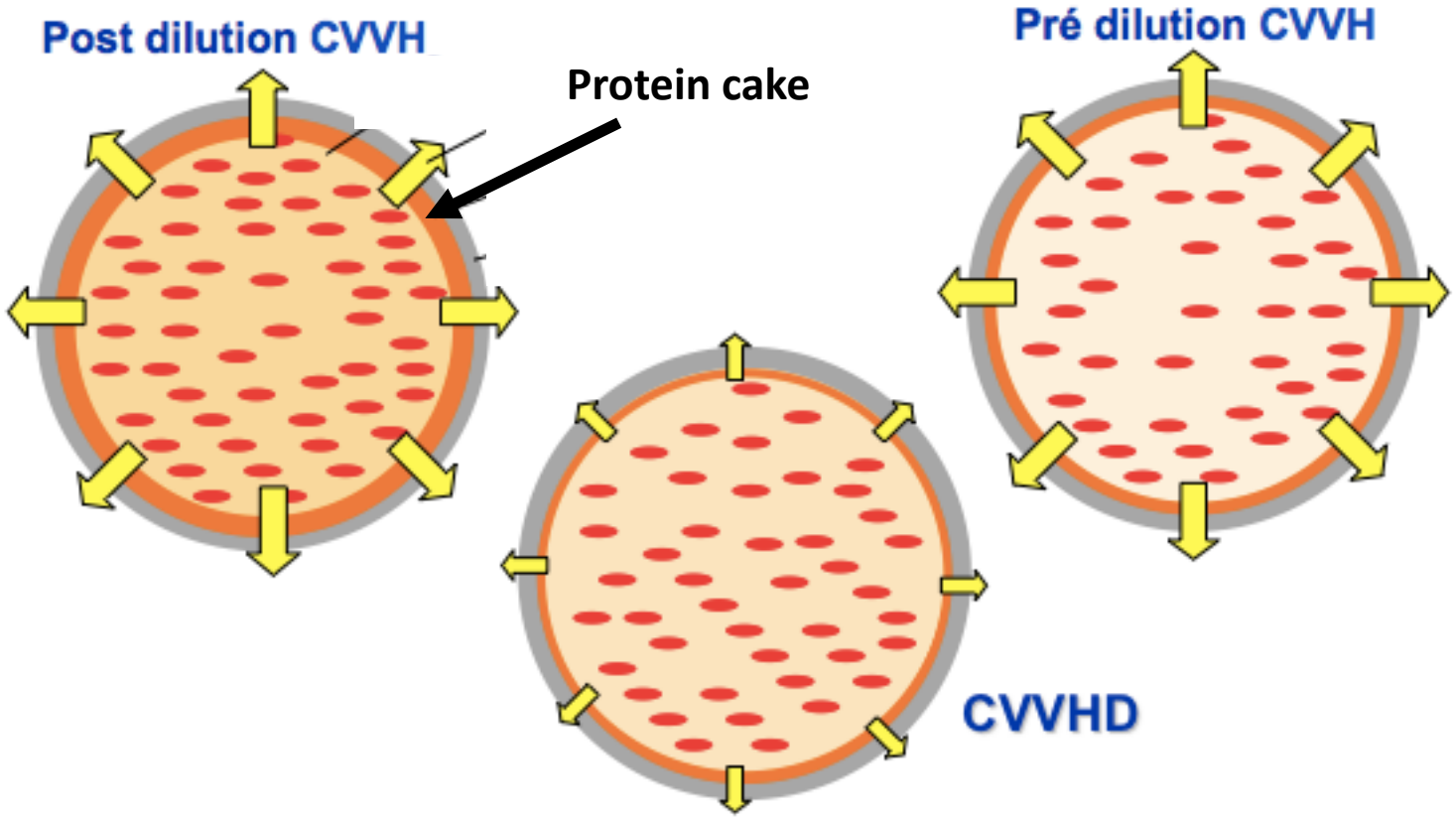
Figure 3. Correlation between clearance reduction and transmembrane pressure is statistically significant with a Spearman's rho of 0.44 ($p < 0.001$).

Zhang et al. ASAIO J 2013

Hemoconcentration in CVVH leads to the formation of protein cake (polarization layer)







CVVH = CALCULATE the filtration fraction when you write the CRRT prescription!

Clogging / Clotting

Membrane clogging	Membrane clotting
= COLMATAGE	
• There is clogging when some blood components accumulate inside the pores of the membrane until they totally block the pores	• There is clotting when clots are large enough to block the capillary fiber
• **=> Permeability is impaired**	• **=> Circulation is impaired**

RRT modality

5.4.6: We suggest not using antibiotic locks for prevention of catheter-related infections of nontunneled dialysis catheters in AKI requiring RRT. (*2C*)

5.5.1: We suggest to use dialyzers with a biocompatible membrane for IHD and CRRT in patients with AKI. (*2C*)

5.6.1: Use continuous and intermittent RRT as complementary therapies in AKI patients. (*Not Graded*)

5.6.2: We suggest using CRRT, rather than standard intermittent RRT, for hemodynamically unstable patients. (*2B*)

5.6.3: We suggest using CRRT, rather than intermittent RRT, for AKI patients with acute brain injury or other causes of increased intracranial pressure or generalized brain edema. (*2B*)

5.7.1: We suggest using bicarbonate, rather than lactate, as a buffer in dialysate and replacement fluid for RRT in patients with AKI. (*2C*)

5.7.2: We recommend using bicarbonate, rather than lactate, as a buffer in dialysate and replacement fluid for RRT in patients with AKI and circulatory shock. (*1B*)

5.7.3: We suggest using bicarbonate, rather than lactate, as a buffer in dialysate and replacement fluid for RRT in

Nothing on CVVHD versus CVVH!

KDIGO guidelines. Kidney Int suppl 2012

RRT modalities: CONCLUSION

The model CVVH/convection/middle molecules *versus* CVVHD/Diffusion/Small molecules is way too simplistic

<u>1- Hemodynamic stability</u>

CRRT+++ The use of CRRT (as the initial modality in the ICU) seems to be associated with better recovery after severe AKI, potentially due to better hemodynamic stability

<u>2- Anticoagulation and CRRT modalities</u>

Citrate should be the first choice for CRRT anticoagulation in most cases
CVVHD allows for an extension of indication thanks to a reduced blood flow rate

<u>3- Filter performance over time</u>

CVVH leads to protein cake. CVVH means filtration fraction to calculate and to pay attention to