

Techniques d'épuration extra-rénale

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- Pas de conflit d'intérêt en lien avec la présentation

Techniques d'épuration extra-rénale

- Mécanismes d'échanges
- Monitoring des pressions
- Modalités intermittentes
- Modalités continues
- Quand débiter l'EER en réanimation ?
- Choix de la modalité intermittente ou continue
- Choix de la modalité parmi les techniques continues
- Choix de la dose
- UF nette
- Prescription



Thomas Graham
1861

Passage de l'urée contenue dans l'urine vers de l'eau à travers une membrane en parchemin



Willem Kolff
1943

Première hémodialyse

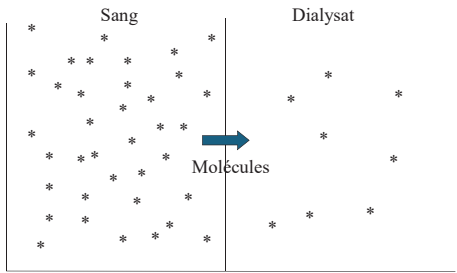


Mécanismes d'échanges à travers la membrane

- Diffusion (loi de Fick) — gradient de concentration
 - Base de l'hémodialyse (HD)
- Convection — gradient de pression hydrostatique transmembranaire
 - Base de l'hémofiltration (HF)
- Adsorption — affinité physico-chimique avec la membrane
 - Interactions hydrophobes, ioniques, forces de Van der Waals
 - Soustraction directe, sans transfert de soluté

Hémodialyse

Hémodialyse



Loi de Fick : $J = -D S dc/dx$

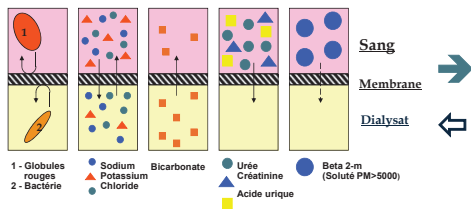
J transfert de masse,
S surface disponible pour les échanges
D coefficient de diffusion du soluté
 dc/dx gradient de concentration

- Principe physico-chimique : DIFFUSION

- Passage d'ions au travers de la membrane semi-perméable selon un **gradient de concentration** : *les ions vont du compartiment le plus concentré vers le compartiment le moins concentré*

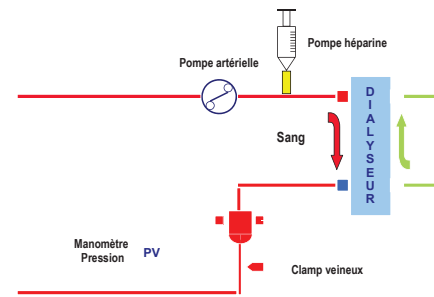
- Intermittente ou continue

Nature des échanges



Diffusion ou dialyse
Transfert moléculaire de solutés
par **Gradient de concentration**

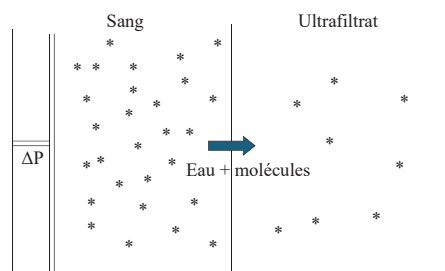
Circuit d'hémodialyse



Hémofiltration

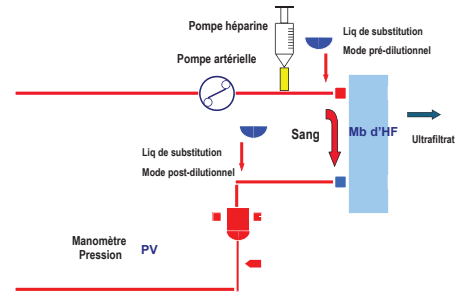


Hémofiltration continue



- Principe physico-chimique : CONVECTION
- Epuration du sang en eau plasmatique et en diverses molécules selon un gradient de pression hydrostatique
- Nécessité d'un liquide de substitution

Circuit d'hémofiltration



Pré et post-dilution

- Pré-dilution :
 - Avantage : diminue le risque de coagulation du filtre
 - Inconvénient : diminue aussi l'efficacité de l'épuration
- Post-dilution :
 - Avantage : augmente l'efficacité de l'épuration
 - Inconvénient : augmente le risque de coagulation du filtre

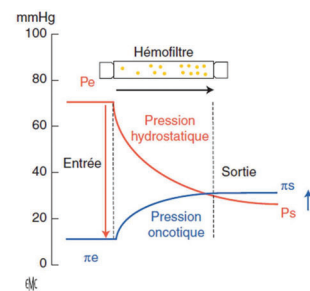


Figure 2. Évolution des pressions au sein de l'hémofiltre en hémo-filtration. La pression hydrostatique (P) diminue progressivement dans l'hémo-filtre par perte de charge tandis que la pression oncotique (π) augmente du fait de l'hémoconcentration. À la sortie de l'hémo-filtre, les deux pressions tendent à s'annuler.

Épuration extrarénale en réanimation, EMC 2025

Fraction de filtration

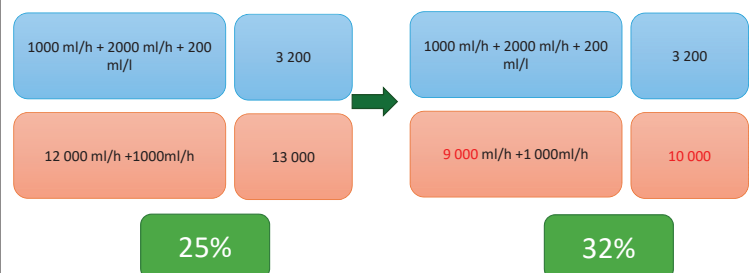
$$\frac{QUF}{Q_{sang} + \text{prédilution}} \longrightarrow \frac{\text{prédilution} + \text{postdilution} + UF \text{ nette}}{Q_{sang} + \text{prédilution}}$$

Cible FF sang (HNF) < 20-25 %
En citrate ?

La fraction de filtration (FF) est un élément fondamental à prendre en compte lors de la prescription d'EERC, en particulier s'il s'agit d'une hémo-filtration continue.

Il est préférable de calculer soi-même la FF « sanguine » en utilisant les formules précisées dans les recommandations nationales et internationales.

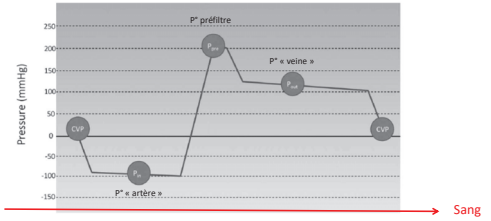
Effet d'une diminution du débit sang



Monitoring des pressions

Pressions

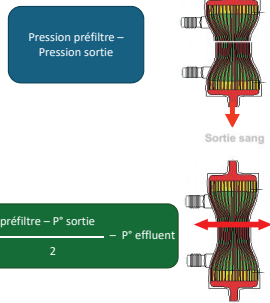
- Mesurées
 - « Artérielle » (P^{in}) : - 50 à - 200 mmHg.
 - « Veineuse » (P^{out}) : + 50 à + 200 mmHg.
 - Pré-filtre ($P^{\text{pré}}$) : + 200 mmHg. Reflet fonctionnement hémofiltre = perméabilité fibres creuses
 - Effluent (P^{eff}) : négative. De + en + négative (cf. clogging/clotting)



Pressions calculées

Perte de charge (pressure drop) :

- Reflet thrombose filtre
- Attention si hausse > 30 mmHg en 4h



Pression trans membranaire (PTM) :

- Gradient de pression entre les 2 cotés de la membrane
- Hausse PTM : clotting et clogging

Clogging / clotting

• Clogging = colmatage

- Hausse lente avec baisse lente P^{eff}
- Reflet saturation des pores
- Touche d'abord les moyennes molécules
- Risque faible de thrombose de filtre au contact via *protein cake*

Hausse isolée PTM
(au début au moins)

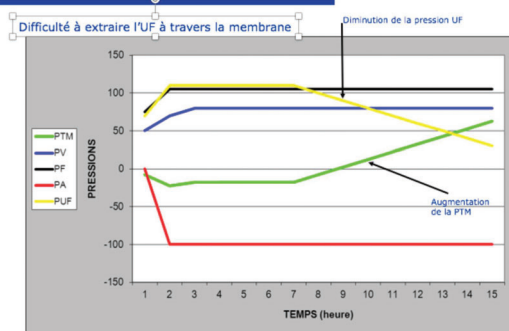
• Clotting = coagulation du circuit

- Hausse brutale
- 2 lieux fréquents : filtre et pièges à bulles veineux
- Pièges à bulles : hausse pression pré filtre et pression de sortie PTM
- Si filtre : hausse pression pré (et perte de charge) puis PTM

Hausse **Pression pré filtre** et PTM

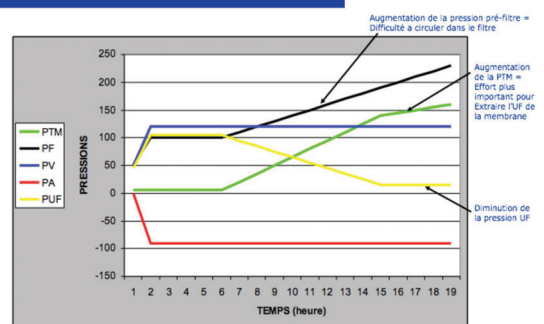
COLMATAGE

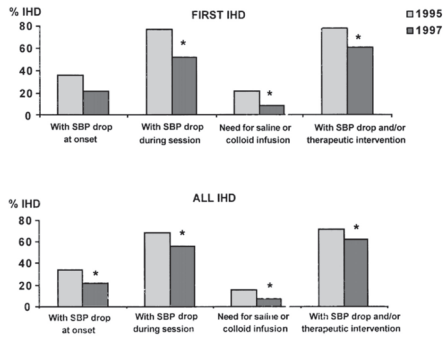
$$PTM = \frac{P_{\text{pre}} + P_{\text{out}}}{2} - P_{\text{eff}}$$



COAGULATION DANS LE FILTRE

$$\Delta P = P_{\text{pre}} - P_{\text{out}}$$





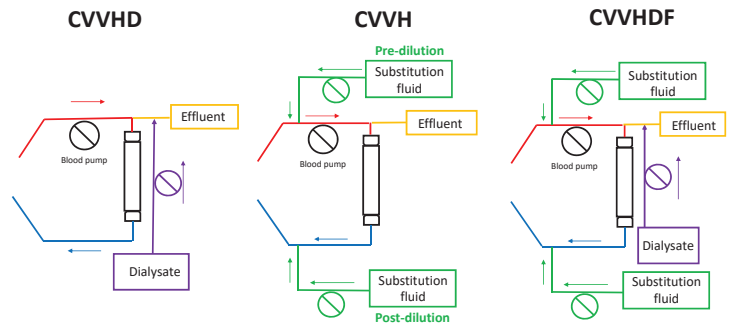
Schortgen et al. AJRCCM 2000

Prescription en pratique de l'HDI en réanimation

- Débit sang : 250 mL/min
- Débit dialysat : 500 mL/min
- Perte de poids = UF nette : cf session spécifique
- Durée : 4 à 6 heures
- Bain de dialyse : K⁺ (et Ca⁺⁺)
- Na⁺, HCO₃⁻ : Na⁺ adapté à la natrémie patient, 10 mmol/L maximum au dessus de la natrémie patient
- Anticoagulation : HBPM, aucune envisageable si risque hémorragique élevé

Modalités continues

Différentes modalités continues



CVVHD : principes

- Lorsque l'HD est réalisée de manière continue, la clairance est dépendante en premier lieu du débit de dialysat
- Clairance = Qd x concentration dialysat sortant/concentration plasmatique
- Pour les petites molécules qui diffusent complètement : Clairance = Qd

CVVH : principes

Lorsque l'hémofiltration est réalisée de manière continue la clairance est dépendante du débit d'ultrafiltrat

$$\text{Clairance} = \frac{Q_s \times (\text{pré} + \text{post} + \text{perte de poids})}{Q_s + \text{pré}}$$

$$\text{Clairance} = Q_{UF} \times SC$$

Où SC est le rapport de la concentration du soluté dans l'ultrafiltrat à sa concentration dans le plasma.

CVVHDF : principes

- Permet de réaliser un transfert de solutés selon les deux mécanismes cités précédemment. En HDF, la dialyse est réalisée en faisant circuler un dialysat à contre-courant par rapport au plasma hémofiltré.

• Quelle utilité ?

L'association d'un transfert convectif à l'HD peut cependant permettre une meilleure clairance des molécules de taille moyenne ou élevée par rapport à une HD seule, ou de diminuer la FF par rapport à une hémofiltration seule, ce qui pourrait s'avérer utile en cas de débit sanguin limité.

Quand débiter l'EER en réanimation ?

Essais cliniques et timing de l'EER

Table 2. Comparison Between Recent Large Randomized Controlled Trials on Optimal Timing of KST in AKI

	ELAIN	AKIKI	IDEAL-ICU	FST	STARRT-AKI	AKIKI2	
No. of patients	231	620	477	118	2,927	278	
Design and countries	Single-center, Germany	Multicenter (31), France	Multicenter (29), France	Multicenter, Thailand	Multicenter (168), 15 countries	Multicenter (39), France	
Recruitment period	2013-2015	2013-2016	2012-2016	2016-2017	2015-2019	2018-2019	
Mean age, y	67	66	69	67	65	65	
Male sex	63%	66%	61%	49%	68%	74%	
Setting	95% surgical (mostly cardiac and abdominal)	80% sepsis	Septic shock	Mixed, 68% medical	67% medical	Received mechanical ventilation and/or vasopressors; 58% septic shock	
Exclusion	CKD stage 4-5, prior KST, KTx, or uncommon causes of AKI	Urgent criteria for KST	Urgent criteria for KST	Baseline Scr ≥ 2 (M) ≥ 1.6 (F) mg/dL, KTx, pregnancy, allergy to loop diuretics, expected death in 24 h or low chance of survival to 28 d, DNR, KST in prior 30 d, sAb < 2 g/dL, ECMO	Urgent criteria for KST, prior KST, advanced CKD (GFR < 20 mL/min/1.73 m ²), KTx, uncommon causes of AKI	Urgent criteria for KST, patients with inclusion criteria already present for > 24 h, CKD stage 4-5, prior KST, KTx, uncommon causes of AKI, Child C liver cirrhosis, pregnancy	Mandatory indication (noticeable hyperkalemia or metabolic acidosis or pulmonary edema) or unit SUN ≥ 140 mg/dL
CKD	41%	10%	16%	NA	44%	12%	

Bouchard et al. AJKD 2021

Essais cliniques et timing de l'EER

Table 2. Comparison Between Recent Large Randomized Controlled Trials on Optimal Timing of KST in AKI

	ELAIN	AKIKI	IDEAL-ICU	FST	STARRT-AKI	AKIKI2
KST modality	CVVHDF 30 mL/kg/h with citrate with transition to SLEDD or IHD	Physician discretion (IHD and CRRT by center [randomized by center])	Physician discretion (IHD and CRRT by center [randomized by center])	CVVH	Physician discretion (IHD and CRRT by center [randomized by center])	Physician discretion (IHD and CRRT, center as a random effect)
Criteria for early KST	Within 8 h of stage 2 and NGAL ≥ 150 ng/mL	Within 6 h of stage 3	Within 12 h of stage 3	Any AKI with absence of response to FST	Within 12 h of stage 2	Stage 3 and oliguria for 72 h or SUN > 112 mg/dL
Criteria for late KST	Within 12 h of stage 3 and NGAL ≥ 150 ng/mL	Urgent criteria: severe hyperkalemia (≥ 6 mmol/L), severe pulmonary edema refractory to diuretics, severe acidosis (pH < 7.15), serum urea > 40 mmol/L, oligoanuria > 72 h	48 h of stage 3	No response to FST and serum urea > 100 mg/dL; severe hyperkalemia (≥ 6 mmol/L), severe metabolic acidosis (pH < 7.15); severe pulmonary edema	AKI for 72 h or conventional criteria: serum K ⁺ ≥ 6.0 mmol/L, pH ≤ 7.20 , or serum HCO ₃ ⁻ ≤ 12 mmol/L, severe respiratory failure (Pao ₂ /Fio ₂ ≤ 200), and clinical perception of volume overload	Mandatory indication (noticeable hyperkalemia or metabolic acidosis or pulmonary edema) or unit SUN ≥ 140 mg/dL
Blinded analysis	No	No	No	No	No	No
Clinical equipoise	No	No	No	No	Yes	No

Bouchard et al. AJKD 2021

Choix de la modalité d'EER



GUIDELINE
Multidisciplinary guidelines on renal replacement therapy in intensive care medicine

REVIEW
Renal replacement therapy in an intensive care unit: guidelines from the SRLF-GFRUP consensus conference

- Practice Point 5.2.1: The initial selection of RRT modality including CRRT, intermittent RRT (IRRT), or acute peritoneal dialysis (PD), should integrate patient characteristics, clinical context, local expertise, and resource availability.
- Recommendation 5.2.1: For critically ill adults with AKI and hemodynamic instability, we suggest using CRRT or acute PD over conventional IRRT.

- 3.1- Continuous or intermittent RRT modality can be used equally to ensure patient survival in severe AKI
- 3.2- We recommend that when selecting the RRT modality the individual clinical situation of the patient be considered, which may justify a preference for either continuous or intermittent therapy
- 3.3- We suggest that in hemodynamically unstable patients with AKI requiring dialysis, continuous or prolonged RRT modalities be preferred to ensure hemodynamic stability and reduce hypotension

The different types of RRT (including continuous, intermittent, or hybrid modalities) should probably be considered equivalent in terms of prognostic criteria. (Grade 2+ /Moderate quality of evidence/ Strong agreement).

EER continue vs HDI : une controverse vieille de 25 ans

EER continue :

- Meilleure stabilité hémodynamique
- Contrôle continu de la volémie
- Contrôle stable des troubles électrolytiques et acido-basiques
- Contrôle thermique
- Évite les variations rapides d'osmolarité et l'œdème cérébral
- Meilleur contrôle de l'urémie

HDI :

- Évite les risques liés à l'anticoagulation continue
- (Mise en œuvre facile au lit du patient)
- Permet une meilleure mobilité du patient
- Moins coûteuse « en soi »



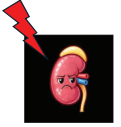
Choix de la modalité : mortalité et récupération rénale

TABLE 1. Primary Analysis Results for Mortality

Comparison	Direct Estimate (95% CI); Certainty of Evidence	Indirect Estimate (95% CI); Certainty of Evidence	Network Estimate (95% CI); Certainty of Evidence*	Plain Text Summary
CRRT vs IHD	1.04 (0.93–1.18); moderate ^a ; 9 studies	NA	1.04 (0.93–1.18); low ^{a,b}	There may be no important difference

TABLE 2. Primary Analysis for Renal Recovery Rate

Comparison	Direct Estimate (95% CI); Certainty of Evidence	Indirect Estimate (95% CI); Certainty of Evidence	Network Estimate (95% CI); Certainty of Evidence*	Plain Text Summary
CRRT vs IHD	1.15 (0.91–1.44); moderate ^a ; 7 studies	NA	1.15 (0.91–1.44); low ^{a,b}	CRRT may increase RRR compared with IHD



Ye et al. Crit Care Explorations 2021

Modalité et récupération rénale

Renal replacement therapy in the ICU: intermittent hemodialysis, sustained low-efficiency dialysis or continuous renal replacement therapy?

Annals of Internal Medicine 2017

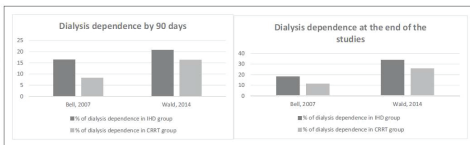


FIGURE 1. Renal recovery at 90 days and the end of follow-up period in Wald et al.'s [27^a] and Bell et al.'s [23] studies.

Renal Replacement Therapy Modality in the ICU and Renal Recovery at Hospital Discharge

Critical Care Medicine 2017

TABLE 3. Multivariate Analyses of the Influence of Intermittent Hemodialysis Versus Continuous Renal Replacement Therapy on Renal Recovery at Hospital Discharge

Variables	OR (95% CI)	p
Main analysis (n = 25,750)	0.910 (0.834–0.992)	0.0327
Propensity score (n = 16,816)	0.883 (0.798–0.975)	0.0144
Only one modality (n = 21,204)	0.893 (0.814–0.988)	0.0244

Variables	Hazard Ratio (95% CI)	p
Mortality as a competitive risk (n = 32,826)	0.958 (0.919–0.997)	0.0375

OR = odds ratio.

Récupération rénale : analyse ancillaire de STARRT AKI

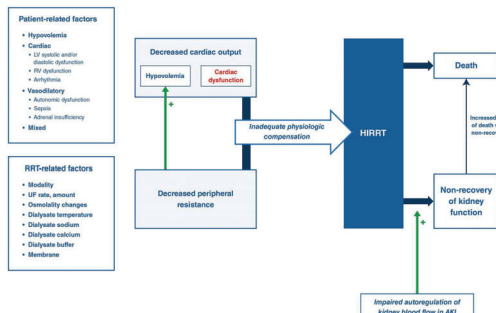
Initiation of continuous renal replacement therapy versus intermittent hemodialysis in critically ill patients with severe acute kidney injury: a secondary analysis of STARRT-AKI trial

Table 2 The association between initial RRT modality and primary and secondary outcomes

Outcome	Number of patients available for analysis				OR or MD (Overlap weighting 95% CI)	p value
	CRRT	IHD	CRRT	IHD		
Primary outcome						
Death or RRT dependence at 90 days, n (%)	1590	606	823 (51.8)	329 (54.3)	0.81 (0.66 to 0.99)	0.044
Secondary outcomes						
All-cause mortality at 90 days, n (%)	1590	606	752 (47.3)	279 (46)	0.90 (0.74 to 1.11)	–
RRT dependence at 90 days (survivors only), n (%)	838	327	71 (8.4)	50 (15.2)	0.61 (0.39 to 0.94)	–
ICU length of stay, days	1590	606	12 (5 to 36)	17 (7 to 165)	–16.8 (–34.3 to 0.7)	–
Hospital length of stay, days	1590	606	27 (10 to 81)	40 (15 to 166)	–14.8 (–32 to 2.5)	–
ICU-free days at 28 days, median (IQR)	1590	606	0 (0 to 17)	0 (0 to 17)	2 (1 to 3)	–
Hospital-free days at 90 days, median (IQR)	1590	606	0 (0 to 56)	0 (0 to 41)	6.6 (3.1 to 10)	–
Ventilator-free days at 28 days, median (IQR)	1590	606	15 (0 to 23)	17 (0 to 25)	0.4 (–0.8 to 1.6)	–
Vasopressor-free days at Day 28, median (IQR)	1590	606	20 (0 to 25)	24 (0 to 27)	–0.7 (–1.9 to 0.5)	–

Pas d'interaction entre le groupe de randomisation et modalité d'EER sur le critère composite mortalité + dépendance à l'EER à J90

Physiopathologie de l'hypotension intra-dialytique



Douvris et al. ICM 2019

Adaptation de la prescription au patient

- Intérêt possible des techniques continues à la phase initiale en cas d'instabilité hémodynamique

Inversement, moins bonne récupération rénale en cas d'exposition prolongée aux techniques continues ?

465 patients were alive at day 90

- 13 were dialysis-dependent
- 53 had a doubling of baseline creatinine

Propensity score matching resulted in 100 well-matched pairs

Predictors of doubling serum creatinine or dialysis at 90 days

Prolonged exposure to CRRT after propensity score matching: OR 3.1 (95% CI; 1.3–8.3 p=0.017)

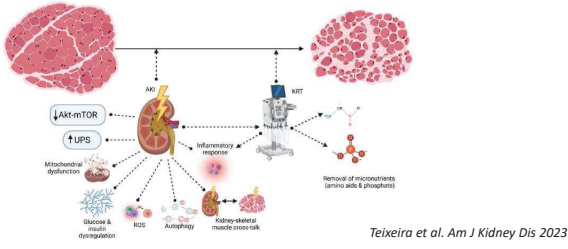
Prolonged exposure to CRRT is independently associated with increased risk of doubling serum creatinine or dialysis at 90 days

Shawwa et al. J Nephrol 2022

Intensive Care Unit–Acquired Weakness in Patients With Acute Kidney Injury: A Contemporary Review

J. Pedro Teixeira, MD^{1,2}, Kirby P. Meyer, DPT, PhD^{2,3}, Benjamin R. Griffin, MD⁴, Nasim George, MD, MPH⁵, Nathaniel Jenkins, PhD⁶, C. Anil Pal, MD¹, Felipe González-Seguel, PT, MSc⁷, Javier A. Neyra, MD, MSc⁸

Diminution de la récupération de la neuromyopathie de réanimation ?



Choix de la modalité : CRRT et HDI complémentaires

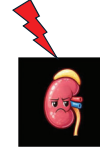
Docteur ?



Machine ?

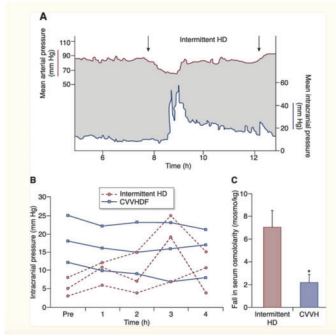


« Le patient à 45 de PAM après branchement de l’HDI »
« Je te prescris de la Noradrénaline »



CRRT et hypertension intracrânienne

CRRT is less likely than IHD to exacerbate intracranial hypertension or to decrease cerebral perfusion pressure.



U.S. National Library of Medicine
ClinicalTrials.gov

Find Studies About Studies

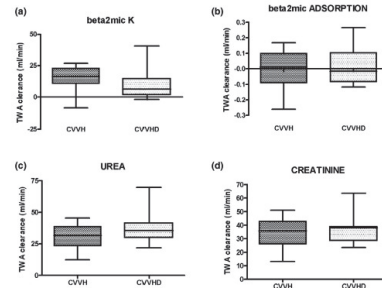
A venir...

IHD Versus CRRT for Severe Acute Kidney Injury in Critically Ill Patients (ICRAKI)

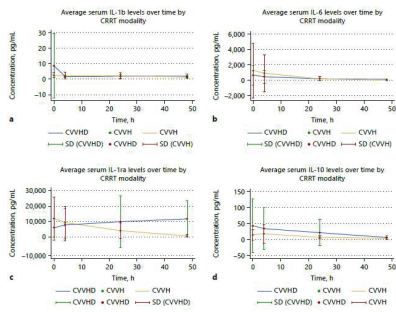
Choix de la modalité parmi les techniques continues

Clairance: convection vs diffusion

Research **Solute removal during continuous renal replacement therapy in critically ill patients: convection versus diffusion** **Open Access** Crit Care 2006
Zaccaro Rocco¹, Claudio Rocchi², Alessandro Bucchieri³, Giuseppe D’Amico⁴, Stefano Rossi⁵, Elias Alessandri⁶, Monica Rocchi⁷ and Paolo Pietrangeli⁸



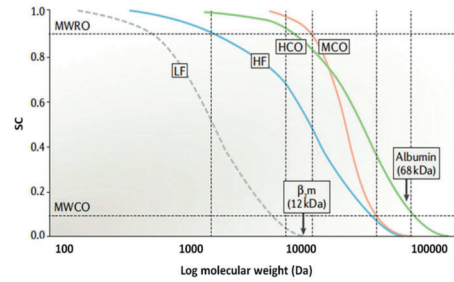
Clairance des cytokines: convection vs diffusion



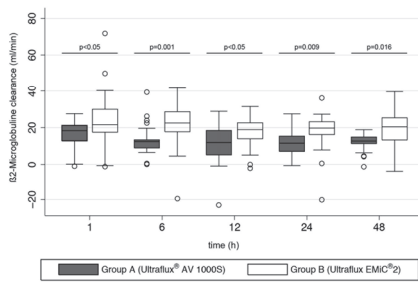
Pas de différence de clairance CVVH en pré-dilution ⚠

Chen et al. Blood Purif 2018

Membranes: l'autre déterminant de la clairance



Optimisation de la clairance en hémodialyse



Meilleure clairance des molécules de poids moléculaire moyen avec SHF que HF

Weidhase et al. Plos One 2019

Hémodiltration vs hémodialyse

Study or Subgroup	Events	Total	Events	Total	Weight	Risk Ratio, 95% CI	Risk Ratio, 95% CI
1.1.1 Survival: Convective Filtration vs Dialysis							
Chen 2008 [25]	7	9	10	11	14.7%	0.88 [0.58, 1.27]	
Mogkova 2008 [24]	6	12	6	12	6.1%	1.00 [0.41, 2.28]	
Chen 2012 [25]	27	38	20	28	14.5%	1.20 [0.71, 1.91]	
Subtotal (95% CI)	40	59	36	51	35.1%	0.96 [0.73, 1.25]	
Total events	25	36	26	36			
Heterogeneity: Tau ² = 0.10; Chi ² = 0.51, df = 2 (P = 0.74); I ² = 5%							
Test for overall effect: Z = 3.28 (P = 0.76)							
1.1.2 Survival: Dose Filtration vs Dialysis Filtration							
Cheng 2009 [27]	26	47	26	49	15.7%	1.04 [0.72, 1.51]	
Subtotal (95% CI)	26	47	26	49	15.7%	1.04 [0.72, 1.51]	
Total events	26	47	26	49			
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.22 (P = 0.83)							
1.1.3 Survival: Dose (Intermediate) Dialysis Filtration vs Dialysis							
PERA 2001 [28]	12	21	4	17	4.6%	2.43 [0.85, 6.18]	
Ruttenmund 2012 [28]	18	27	18	33	8.6%	0.88 [0.38, 1.22]	
Subtotal (95% CI)	30	48	22	50	13.4%	1.22 [0.55, 2.62]	
Total events	30	48	22	50			
Heterogeneity: Tau ² = 0.85; Chi ² = 5.15, df = 1 (P = 0.02); I ² = 81%							
Test for overall effect: Z = 3.31 (P = 0.76)							
1.1.4 Filtration vs Higher Dose Dialysis Filtration							
Cheng 2009 [27]	7	9	11	15.2%	1.07 [0.73, 1.57]		
Subtotal (95% CI)	7	9	11	15.2%	1.07 [0.73, 1.57]		
Total events	7	9	11	15.2%			
Heterogeneity: Tau ² = 0.05; Chi ² = 2.76, df = 1 (P = 0.10); I ² = 64%							
Test for overall effect: Z = 1.47 (P = 0.14)							
Total (95% CI)	265	295	275	306.0%	1.10 [0.88, 1.38]		
Total events	157	136	136	100.0%			
Heterogeneity: Tau ² = 0.05; Chi ² = 13.88, df = 7 (P = 0.05); I ² = 50%							
Test for overall effect: Z = 3.02 (P = 0.003)							
Test for subgroup differences: Chi ² = 1.97, df = 3 (P = 0.56), I ² = 6%							

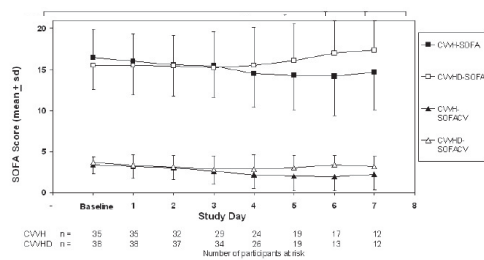
19 RCTs (before 2012)
 ➤ Small sample size
 ➤ High heterogeneity

Figure 2 Effect of hemofiltration vs hemodialysis RRT on mortality. The pooled risk ratio was calculated using a random-effects model. Weight refers to the contribution of each study to the overall estimate of treatment effect. Abbreviations: CI, confidence interval; N, number of patients.

Friedrich et al. Critical Care 2012

CVVH vs CVVHD: RCT

OMAKI pilot study: CVVHD vs CVVH with pre and post dilution
 39 vs 38 patients



Wald et al. Critical Care 2012

CVVH vs CVVHDF: RCT

102 patients: CVVH 25 ml/Kg/h vs
 104 patients: CVVHDF 25 + 18 ml/Kg/h in pre dilution mode

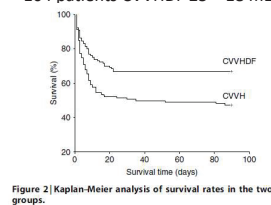


Figure 2 Kaplan-Meier analysis of survival rates in the two groups.

➔ Small sample size
 ➔ Low prescribed dose in CVVH group

Variable	Unadjusted HR	P-value	Adjusted HR	P-value
Age	1.01 (0.99-1.03)	0.07	1.02 (1.00-1.04)	0.01
Gender	0.80 (0.54-1.18)	0.26	0.70 (0.44-1.09)	0.12
Weight	1.00 (0.99-1.01)	0.91	1.00 (0.99-1.01)	0.71
Diagnosis				
Surgical	1	0.32	1	0.12
Trauma	1.48 (0.68-3.19)	0.43	1.88 (0.84-4.19)	0.19
Medical	1.21 (0.76-1.92)	0.44	1.40 (0.85-2.29)	0.19
Sepsis	1.53 (1.02-2.30)	0.04	1.30 (0.50-1.20)	0.24
Baseline BUN	0.98 (0.97-0.99)	0.02	0.98 (0.97-0.99)	0.008
CVVHDF vs CVVH	0.40 (0.31-0.73)	0.001	0.59 (0.40-0.87)	0.008
APACHE II score	1.07 (1.04-1.09)	0.001	1.06 (1.03-1.08)	0.001

Saudan et al. Kidney International 2006

En chronique: CONVINC TRIAL

Table 2. Primary and Secondary Outcomes.^a

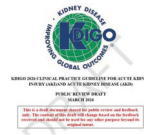
Variable	High-Dose Hemodiafiltration (N=683)		High-Flux Hemodialysis (N=677)		Hazard Ratio (95% CI) ^b
	no. (%)	no. of events/100 patients-yr (95% CI)	no. (%)	no. of events/100 patients-yr (95% CI)	
Primary outcome					
Death from any cause	118 (17.3)	7.13 (5.90–8.54)	148 (21.9)	9.19 (7.77–10.79)	0.77 (0.65–0.93)
Secondary outcomes					
Death					
Cardiovascular	31 (4.5)	1.87 (1.27–2.66)	37 (5.5)	2.30 (1.62–3.17)	0.81 (0.49–1.33)
Noncardiovascular	87 (12.7)	5.26 (4.21–6.48)	111 (16.4)	6.89 (5.67–8.30)	0.76 (0.59–0.98)
Infection-related					
Including Covid-19	18 (5.6)	2.30 (1.62–3.15)	54 (8.0)	3.35 (2.52–4.37)	0.69 (0.49–0.96)
Excluding Covid-19	23 (3.4)	1.39 (0.88–2.09)	33 (4.9)	2.05 (1.41–2.88)	0.68 (0.42–1.10)

Blankestijn et al. NEJM 2023

Choix de la dose

Définition de la dose d'EER

- La notion de dose de dialyse est d'abord un concept utilisé chez le patient insuffisant rénal chronique pour juger de l'efficacité d'une séance de dialyse chronique.
- En dialyse chronique, la dose de dialyse est donc définie par le produit de la clairance (K) multiplié par le temps (t), c'est-à-dire au transfert de masse dans un intervalle de temps donné (la durée de la séance d'EER). Il est rapporté au volume (V) de distribution théorique du patient, afin de s'adapter au poids de chaque patient et donc au volume dans lequel se dilue l'urée plasmatique : Kt/V
- Non applicable en AKI : volume de distribution de l'urée modifié
- Dose en EERC exprimée en ml/kg/h (poids ajusté)**
 - CVVH : dose = débit d'ultrafiltration
 - CVVHD : dose = débit de dialysat
 - CVVHDF : dose = débit de dialysat + débit d'ultrafiltration



Recommendation 5.3.1: We recommend **delivering an effluent volume of 20-25 ml/kg/h** over higher volumes for solute clearance in adults receiving CRRT, or a Kt/V of 3.9 per week over higher urea clearance in adults receiving IRRT or PIRRT for AKI (1B).

Practice Point 5.3.1: An initial CRRT dose-intensity for adults with high body mass index (BMI; e.g., ≥ 30 kg/m²) based on **ideal or adjusted body weight**, rather than actual body weight, can be used to avoid delivery of excess CRRT dose-intensity.

Recommendation 5.3.2: We recommend **not prescribing high-volume hemofiltration (HVHF)** compared with standard CRRT dose-intensity for critically ill adults with AKI in the setting of sepsis or septic shock (1B).

5.1- We recommend that for continuous RRT a dose of 20–25 ml/kg/h be administered

Dose et mortalité

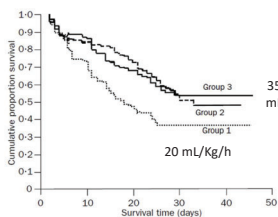


Figure 2: Kaplan Meier estimation of survival rates in the three groups

Variable	Unadjusted hazard ratio (95% CI)	Adjusted hazard ratio (95% CI)
Sex (female)	0.90 (0.69–1.19)	0.89 (0.66–1.20)
Weight	1.01 (0.99–1.03)	1.00 (0.99–1.02)
Age	1.00 (0.98–1.01)	1.00 (0.98–1.01)
Causes of acute renal failure		
Surgical	1.0	1.0
Medical	0.483 (0.28–0.82)	0.82 (0.46–1.46)
Trauma	1.384 (0.93–2.06)	1.09 (0.72–1.64)
Presence of sepsis	1.71 (1.20–2.44)	0.55 (0.34–0.89)
BUN at start of continuous haemofiltration	1.06 (1.05–1.07)	1.05 (1.04–1.07)
APACHE II score	1.13 (1.09–1.18)	1.11 (1.04–1.19)
Trial groups		
Group 1	1.0	1.0
Group 2	0.55 (0.40–0.77)	0.51 (0.36–0.72)
Group 3	0.57 (0.41–0.78)	0.49 (0.35–0.69)

Table 2: Results of Cox's proportional hazards regression

Ronco et al. Lancet 2000

Dose et mortalité

ATN Study, NEJM 2008

Table 3. Primary and Secondary Outcomes.^a

Outcome	Intensive Strategy (N=403)	Less Intensive Strategy (N=345)	ORs Ratio or Mean Difference (95% CI)	P Value
	Death from any cause by day 60 — no. (%)	302 (33.6)	289 (51.5)	
In-hospital death — no. (%)	288 (31.2)	269 (48.0)	1.15 (0.90 to 1.47)	0.27
Discharged to home, off dialysis, by day 60 — no./no. with data (%)	88/540 (15.7)	92/561 (14.4)	0.95 (0.68 to 1.32)	0.75
Recovery of kidney function by day 28 — no./no. with data (%) ^b	85/553 (15.4)	102/555 (18.4)	0.83 (0.62 to 0.87)	0.24
Complete	49/553 (8.9)	50/555 (9.0)		
Partial	435/553 (78.6)	405/555 (72.6)		

- IHD : 3 vs 6 / week
- CVVHDF : 20 vs 35 mL/kg/h

RENAL Study, NEJM 2009

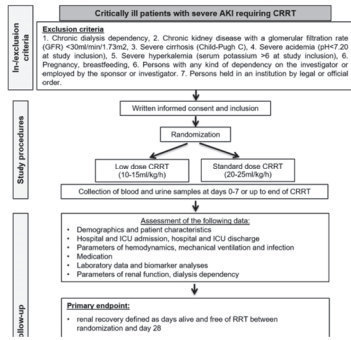
Table 1. Primary and Secondary Outcomes.^a

Outcome	Higher-Intensity CRRT	Lower-Intensity CRRT	ORs Ratio (95% CI)	P Value ^b
Death — no./total no. (%)				
By day 90	322/722 (44.7)	332/763 (43.7)	1.00 (0.81–1.23)	0.99
By day 28	270/722 (37.5)	274/763 (36.0)	1.07 (0.81–1.42)	0.52
Place of death — no./total no. (%)				
ICU	251/722 (34.8)	254/763 (33.3)	1.06 (0.82–1.27)	0.61
Hospital ward	60/722 (8.4)	76/763 (10.0)	0.81 (0.64–1.00)	0.40
Outside hospital, after discharge	1/722 (0.14)	2/763 (0.3)	1.54 (0.25–9.27)	0.63
RRT dependence among survivors				
At day 28	44/443 (10.4)	57/469 (12.2)	1.22 (0.81–1.77)	0.31
At day 90	27/399 (6.8)	34/413 (8.4)	1.59 (0.84–2.92)	0.14

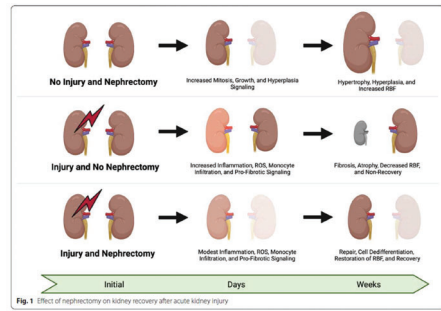
- CVVHDF : 25 vs 40 mL/kg/h

Vers une adaptation personnalisée de la dose ?

BMJ Open Randomised controlled study investigating standard dose continuous renal replacement therapy (CRRT) versus low-dose CRRT in critically ill patients with acute kidney injury (AKI): study protocol for a prospective, randomised, controlled, international, multicentre trial (the 'Ketzerel' trial)

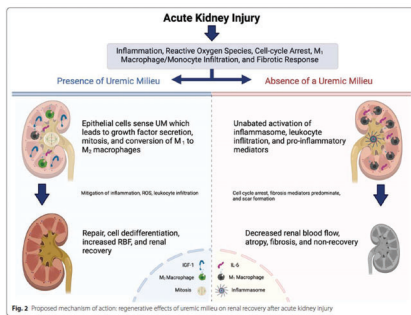


Concept d'azotémie permissive



Chawla Critical Care 2022

Concept d'azotémie permissive

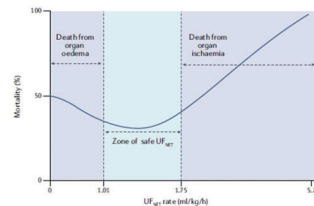


Chawla Critical Care 2022

UF nette ou « perte de poids »

UF nette optimale ?

Study population	No. of patients	Exposure UF _{net} rate	Comparator UF _{net} rate	Key findings	Ref.
AKI + >SFD + HD + CVVHD	1,075	>25 ml/kg/day	<20 and 20-25 ml/kg/day	1.1-year mortality	13
AKI + CVVHD	1,434	>1.75 ml/kg/h	<1.01 and 1.01-1.75 ml/kg/h	1.90-day mortality	47
AKI + CVVH	1,398	>35 ml/kg/day	<35 ml/kg/day	1.30-day mortality	76
AKI + CVVHDF	347	>1.75 ml/kg/h	<1.01 and 1.01-1.75 ml/kg/h	1.28-day hospital mortality	66
AKI + CVVHDF	347	>1.75 ml/kg/h	<.01 and 1.01-1.75 ml/kg/h	Direct causal effect of UF _{net} rate >1.75 ml/kg/h on mortality not mediated by fluid balance or haemodynamics	11
AKI survivors	100	Higher LFR	Lower LFR	1 Dialysis dependence at 90 days among survivors	82
AKI + CRT	157	Higher LFR	Lower LFR	1 Dialysis dependence among survivors	88

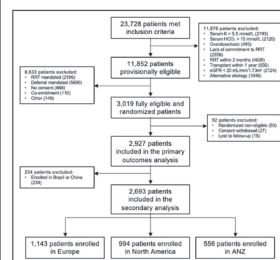


Murugan et al. Nature reviews nephrology 2020

Analyse ancillaire de STARRT-AKI: différences selon zone géographique d'inclusion

Regional Practice Variation and Outcomes in the Standard Versus Accelerated Initiation of Renal Replacement Therapy in Acute Kidney Injury (STARRT-AKI) Trial: A Post Hoc Secondary Analysis

Vaara et al. Critical care explorations 2024



Paramètres étudiés

- 1/ Fluid balance
- 2/ Timing d'initiation dans le groupe standard
- 3/ Modalité d'EER

Characteristic	North America (n = 994)	Europe (n = 1143)	Australia and New Zealand (n = 556)	p
Age, yr	65.4 (56.7-73.5)	68.4 (58.9-76.0)	66.7 (56.6-75.0)	< 0.001
Male gender	672 (67.6)	795 (69.6)	367 (66.0)	0.293
Weight, kg	89.0 (73.6-108.0)	82.0 (70.5-95.0)	87.0 (73.6-102.4)	< 0.001
Simplified Acute Physiology Score II	62.0 (50.0-74.0)	55.0 (44.0-69.0)	61.0 (47.0-74.2)	< 0.001
Hours between randomization and renal replacement therapy	7.5 (4.2-26.0)	12.1 (8.7-32.3)	22.6 (19.3-36.8)	< 0.001
Accelerated arm	5.1 (3.2-7.0)	9.3 (7.9-11.8)	6.3 (4.2-9.0)	< 0.001
Standard arm	28.9 (21.0-58.9)	52.5 (29.8-84.0)	40.9 (31.1-63.3)	< 0.001
Type of admission				< 0.001
Medical	686 (69.0)	854 (74.7)	267 (48.0)	
Scheduled surgery	114 (11.5)	108 (9.4)	116 (20.9)	
Unscheduled surgery	194 (19.5)	181 (15.8)	173 (31.1)	
Pre-randomization clinical frailty score	3.0 (2.0-4.0)	2.0 (0.0-4.0)	3.0 (1.0-4.0)	< 0.001
Pre-randomization support				< 0.001
Mechanical ventilation or continuous positive airway pressure	807 (80.9)	864 (75.6)	440 (79.1)	
Norepinephrine use	645 (64.6)	726 (63.5)	410 (73.7)	< 0.001
Norepinephrine dose, µg/kg/min	0.2 (0.1-0.3)	0.3 (0.1-0.7)	0.2 (0.1-0.3)	< 0.001
Diuretic use	340 (34.2)	289 (25.3)	233 (41.9)	< 0.001

Europe : patients plus âgés, motif admission médical

ANZ : post opératoire de chirurgie cardiaque, support vasopresseur, moins de sepsis

Amérique : ventilation mécanique

Contrôle du fluid balance selon région

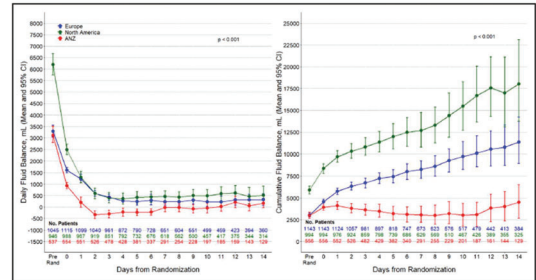


Figure 2. Daily and cumulative fluid balance according to geographical regions. ANZ = Australia and New Zealand.

Surcharge plus importante en Amérique et Europe vs ANZ

Différence à la randomisation et qui s'accroît des J1 entre ANZ vs Europe/Amérique

Table 3 - Fluid Balance in the First 14 Days Across Geographic Regions in the Medical and Surgical Patient Subgroups.

	Medical Patients				Surgical Patients			
	North America (n = 686)	Europe (n = 854)	ANZ (n = 267)	p value	North America (n = 308)	Europe (n = 289)	ANZ (n = 289)	p value
Fluid balance, mL								
Mean daily	537.6 (-288.9 - 1265.1)	487.7 (-189.4 - 1408.2)	495.5 (-59.3 - 507.4)	< 0.001	122.4 (-419.7 - 969.2)	298.3 (-374.2 - 927.8)	-34.9 (-520.2 - 509.5)	0.002
Median daily	333.0 (-315.8 - 1147.0)	510.0 (-179.0 - 1444.5)	520.0 (-438.5 - 425.5)	< 0.001	108.5 (-515.2 - 794.6)	217.0 (-301.6 - 922.0)	100.5 (-461.0 - 579.5)	0.129
Total	2354.5 (-2598.5 - 9582.2)	3281.0 (-1383.8 - 9942.5)	476.0 (-4586.5 - 3342.5)	< 0.001	781.0 (-3783.8 - 7388.2)	1986.0 (-1099.0 - 6870.0)	-310.0 (-4162 - 3603)	0.002
Fluid balance*, mL								
Mean daily	820.1 (130.5 - 1842.1)	695.9 (32.4 - 1711.4)	203.2 (-294.5 - 785.7)	< 0.001	724.1 (26.8 - 1692.0)	612.6 (26.3 - 1223.2)	305.0 (-132.9 - 798.1)	< 0.001
Median daily	496.5 (-733.3 - 1387.2)	630.0 (-49.8 - 1513.2)	119.0 (-261.9 - 946.5)	< 0.001	291.3 (-207.1 - 1062.2)	348.0 (-196.2 - 1019.2)	163.5 (-241.0 - 661.0)	0.094
Total	7608.5 (1123.0 - 16559.0)	6879.5 (794.5 - 14630.5)	2138.0 (-2332.0 - 6179.0)	< 0.001	6603.0 (240.2 - 15724.8)	8222.0 (119.0 - 11566.0)	3274.0 (-1103 - 6994)	< 0.001

Data are median (quartile 25* - quartile 75*) or N (%).

* Including pre-randomization fluid balance

Fluid Balance plus élevé aux USA et en UE : concerne patients médicaux et chirurgicaux

Modalité initiale selon région

TABLE 1. Baseline Characteristics

Characteristic	North America (n = 994)	Europe (n = 1143)	Australia and New Zealand (n = 556)	p
Initial modality				< 0.001
Continuous renal replacement therapy	481 (60.8)	492 (56.8)	422 (95.7)	
Intermittent hemodialysis	238 (30.1)	361 (41.7)	3 (0.7)	
Sustained low-efficiency daily dialysis	72 (9.1)	13 (1.5)	16 (3.6)	

➤ Presque 100% CRRT en ANZ

➤ Explique un meilleur contrôle de la balance hydrosodée chez les patients en ANZ ?

Analyse multivariée comparant différentes régions

➔ Ajustement sur âge, sexe, score SAPS II, type d'admission, sepsis

TABLE 4. Multivariable Models for Key Outcomes

Outcome	North America vs. Europe		ANZ vs. Europe		ANZ vs. North America	
	Effect Estimate (95% CI)	p	Effect Estimate (95% CI)	p	Effect Estimate (95% CI)	p
90-d mortality (RD)	-0.37 (-6.32 to 5.60)	0.904	-11.31 (-17.74 to -4.85)	0.001	-10.27 (-17.47 to -3.07)	0.007
ICU mortality (RD)	-0.18 (-5.61 to 5.26)	0.949	-11.63 (-17.69 to -5.57)	< 0.001	-11.66 (-18.02 to -5.29)	0.001
Hospital mortality (RD)	0.39 (-5.25 to 6.05)	0.892	-10.96 (-16.95 to -4.97)	0.001	-10.98 (-17.92 to -4.06)	0.003
RRT dependence at day 90 (RD)	2.81 (-1.76 to 7.39)	0.234	-4.61 (-9.72 to 0.52)	0.083	-7.85 (-11.38 to -4.31)	< 0.001
Death or RRT dependence at day 90 (RD)	-0.34 (-6.36 to 5.68)	0.911	-11.56 (-18.10 to -4.99)	0.001	-10.50 (-17.74 to -3.24)	0.006
ICU-free days at day 28 (MD)	0.51 (-1.40 to 2.43)	0.599	5.86 (3.40-8.33)	< 0.001	4.72 (1.82-7.63)	0.001
Hospital-free days at day 90 (MD)	-0.50 (-6.54 to 5.36)	0.846	18.38 (9.74-27.03)	< 0.001	17.27 (7.12-27.43)	0.001
Ventilator-free days at day 28 (MD)	0.31 (-2.28 to 2.91)	0.812	6.27 (3.41-9.14)	< 0.001	5.72 (2.53-8.91)	< 0.001
RRT-free days at day 90 (MD)	-5.03 (-15.41 to 5.35)	0.342	18.74 (9.94-31.53)	0.004	25.67 (8.94-42.41)	0.003

Meilleurs outcome dans chez les patients traités en ANZ

Résultats confirmés si exclusion des patients en post opératoire de chirurgie cardiaque

France vs Europe

Table 14 - Summary of baseline characteristics between France and the rest of Europe

	France (n = 747)	Rest of Europe (n = 396)	p value
Hours between eligibility and RRT	8.4 (4.0 - 32.2)	9.6 (5.4 - 27.1)	0.301
Accelerated arm	5.1 (3.1 - 8.3)	6.4 (3.9 - 8.6)	0.030
Standard arm	63.7 (27.5 - 87.9)	33.3 (21.4 - 62.0)	< 0.001
Premorbid creatinine, µmol/L	99.0 (73.0 - 141.0)	90.0 (70.7 - 123.8)	0.004
eGFR, mL/min/1.73 m ²	62.4 (40.6 - 88.6)	70.2 (47.9 - 92.1)	0.001
eGFR < 60, mL/min/1.73 m ²	390 (52.2)	244 (61.6)	0.003
Initial modality - no. (%)			< 0.001
CRRT	222 (40.2)	270 (68.0)	
IHD	325 (58.9)	36 (11.5)	
SLED	5 (0.9)	8 (2.5)	
Fluid balance, mL			
Mean daily	645.0 (-64.2 - 1601.4)	139.7 (-388.2 - 743.5)	< 0.001
Median daily	680.0 (-75.0 - 1570.5)	83.0 (-435.0 - 634.1)	< 0.001
Total	4100.0 (-429.5 - 12313.0)	1101.5 (-3306.2 - 5666.8)	< 0.001

Pas de différence notable sur score de gravité, plus d'admissions médicales, moins de défaillance cardiovasculaire en France

France vs Europe : analyse multivariée

eTable 17 - Full Multivariable Models for Key Outcomes (France vs. rest of Europe)

	France (n = 747)	Rest of Europe (n = 396)	Effect Estimate (95% CI)	p value
90-day mortality (RD)	367 / 747 (49.1)	147 / 396 (37.1)	12.22 (4.46 to 19.96)	0.004
ICU mortality (RD)	282 / 747 (37.8)	107 / 396 (27.0)	11.17 (3.82 to 18.51)	0.006
Hospital mortality (RD)	330 / 746 (44.2)	131 / 396 (33.1)	11.53 (4.69 to 18.31)	0.003
RRT dependence at day 90 (RD)	30 / 376 (8.0)	19 / 246 (7.7)	1.69 (-5.71 to 9.06)	0.665
Death or RRT dependence at day 90 (RD)	397 / 743 (53.4)	166 / 393 (42.2)	12.24 (4.38 to 20.09)	0.004
ICU-free days at day 28 (MD)	0.0 (0.0 - 20.0)	8.0 (0.0 - 22.0)	-3.49 (-5.77 to -1.21)	0.003
Hospital-free days at day 90 (MD)	0.0 (0.0 - 60.0)	28.0 (0.0 - 65.2)	-8.39 (-16.46 to -0.31)	0.042
Ventilator-free days at day 28 (MD)	5.0 (0.0 - 23.8)	13.5 (0.0 - 24.0)	-3.95 (-6.63 to -1.28)	0.004
RRT-free days at day 90 (MD)	0.0 (0.0 - 89.0)	73.0 (0.0 - 88.0)	-15.37 (-28.01 to -2.73)	0.017

Différence de mortalité non expliquée par le timing de l'EER mais peut-elle être expliquée par d'autres facteurs de réalisation de l'EER : modalité + contrôle du FB ?

Exemples de prescription

Exemples de prescription

	CVVHD	CVVH	CVVHDF
Dose délivrée	20 – 25 mL/Kg/h	20 – 25 mL/Kg/h	20 – 25 mL/Kg/h
Débit sang	80 à 150 mL/min	100-250 mL/min	100-200 mL/min
Pré-dilution	0	Selon anticoagulation	Selon anticoagulation
Post-dilution	0	Selon anticoagulation	Préférer post-dilution pour optimiser clairance 10 à 15 mL/Kg/h
Dialysat	20-25 mL/Kg/h	0	10 à 15 mL/Kg/h
UFnette	Selon tolérance hémodynamique		



Si anticoagulation au citrate, asservissement de la quantité de citrate administrée au débit sang

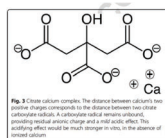
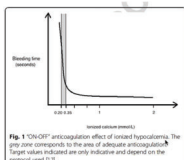
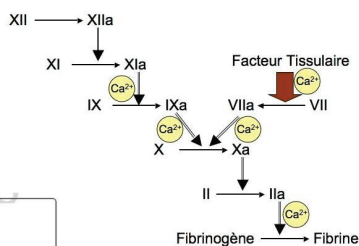
Anticoagulation



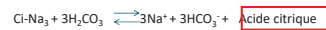
• **Recommandation 5.5.1:** Where available, we recommend using regional citrate anticoagulation rather than heparin in children and adults receiving CRRT who do not have contraindications to citrate

- Citrate utile surtout en CRRT.
- HBPM à dose préventive voire pas d'anticoagulation en HDI

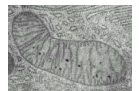
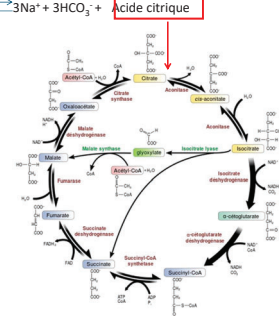
Anticoagulation régionale au citrate



Métabolisme du citrate



CYCLE DE KREBS
« Citric acid cycle »



Foie +++
Rein
Muscles

Elimination du citrate au cours d'une EER

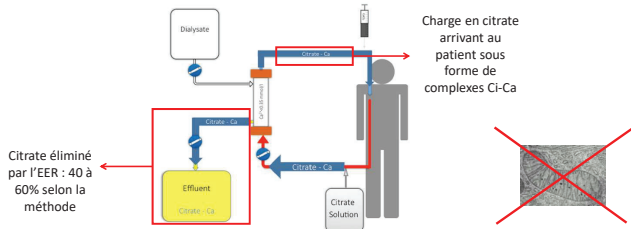
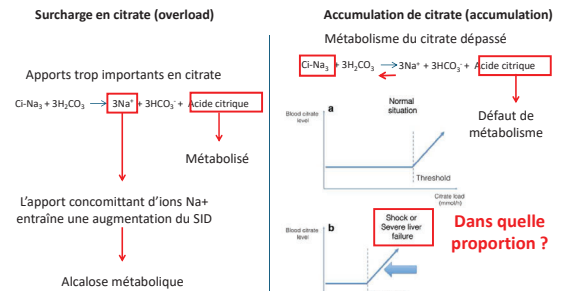


Fig. 2 Schematic view of a CRRT circuit with regional citrate administration in CVHD mode. Alternative modes can be used (postdilution CVHD, postdilution pre and postdilution CVHD, CVHCA, etc.) according to the protocol used. Citrate solution is administered at the beginning of the CRRT circuit. It forms citrate-calcium complexes, which are largely removed from the blood at the level of the filter. Only complexes which are not removed through the hemofilter return to the patient's blood and need to be metabolized.

Complications au cours de l'administration de citrate



Schneider et al. Critical care 2017

Accumulation de citrate: diagnostic

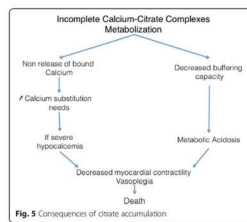
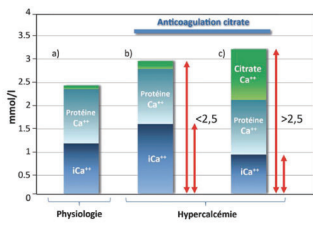
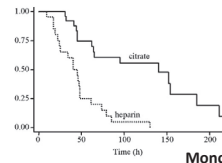
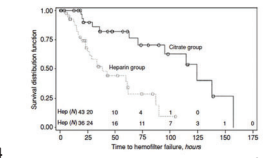


Fig. 5 Consequences of citrate accumulation

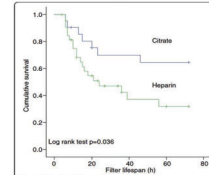
Citrate et durée de vie des hémo-filtres



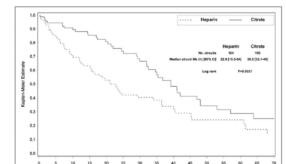
Monchi et al. ICM 2004



Kutsogiannis et al. Kidney Int 2005



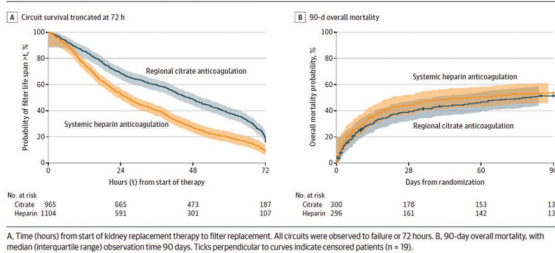
Stucker et al. Crit Care 2015



Gattas et al. Crit Care Med 2015

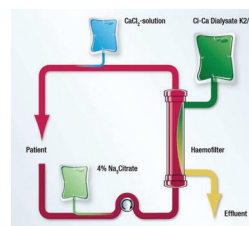
Citrate et mortalité

Figure 2. Kaplan-Meier Curves With Hall-Welsher Confidence Bands



A. Time (hours) from start of kidney replacement therapy to filter replacement. All circuits were observed to failure or 72 hours. B. 90-day overall mortality, with median (interquartile range) observation time 90 days. Ticks perpendicular to curves indicate censored patients (n = 19).

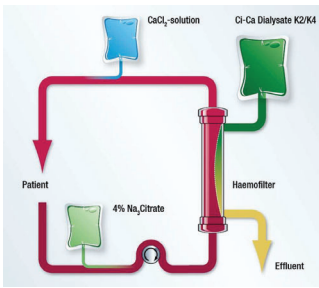
CVHD citrate



Name	D/GB/F/UR/ N/C/R/S/N/W/ CZ/SR/SK/TR	R/US/EST/ L/TAL/W/SH	Na ⁺ mmol/L	K ⁺ mmol/L	Ca ²⁺ mmol/L	Mg ²⁺ mmol/L	Cl ⁻ mmol/L	HCO ₃ ⁻ mmol/L	Inorganic Phos- phate mmol/L	Glucose g/L
Cl-Ca ²⁺ Dialysate K2 (Plus)	F00001624	F00000075	133	2	0	1	115.75	20	1.25	1
Cl-Ca ²⁺ Dialysate K4 (Plus)	F00001625	F00000080	133	4	0	1	117.75	20	1.25	1

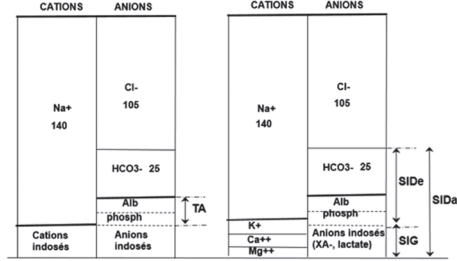
Composition du dialysat calculée pour maintenir équilibre acido-basique avec un rapport Qs / Qd de 1/20
 Qs = 100 mL/min et Qd = 2000 mL/h

En anticoagulation au citrate, toute modification de ce rapport tend à modifier l'équilibre acido-basique.



Na 133mmol/L, K 2/4 mmol/L, Mg 1 mmol/L, Cl 115mmol/L, HCO3- 20mmol/L, Phosphore 1,25mmol/L, Glucose 1g/L 0 Ca
=> Diminution du SID = effet acidifiant

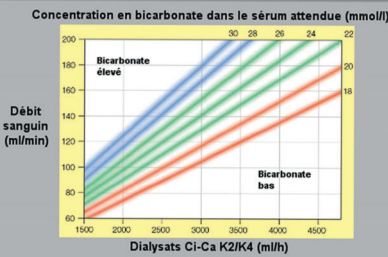
Apport Cl + 3Na concentré (136mmol/L de Cl), asservi au débit de sang
=> Augmentation du SID = effet alcalinisant



Le SID est la différence entre cations forts (Na+ principalement) et anions forts plasmatiques (Cl- principalement). Il exerce un pouvoir alcalinisant sur le plasma.

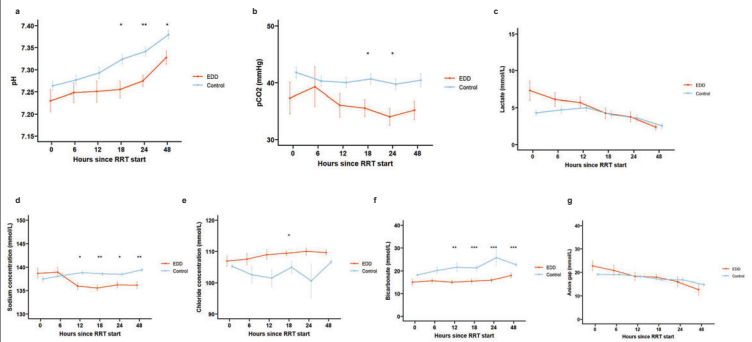
Le SID apparent (SIDa) = $Na^+ + K^+ + Mg^{++} + Ca^{++} - (Cl^- + lactate + anions\ forts\ indosés)$ est augmenté par l'apport de sodium

Effet typique du débit sanguin et du débit de dialysat sur l'équilibre acido-basique



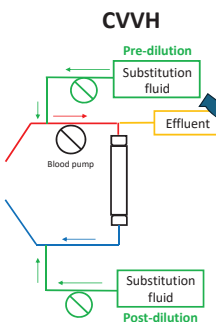
Graphique créé selon les paramètres de traitement suivants : dose de citrate 4,0 mmol/l, dose de Ca 1,7 mmol/l, taux d'UF net 100 ml/h Variabilité entre les patients non prise en compte.

Qs, Qd et modification de l'équilibre acido-basique



Bidar et al. ACCPM 2025

CVVH citrate



COMPOSITION DES SOLUTIONS**	REGIOCIT (mmol/l)	PHOXILUM (mmol/l)	BIPHOSZYL (mmol/l)
Citrate	18	0	0
Bicarbonate	0	30	22
Sodium	140	140	140
Potassium	0	4	4
Magnésium	0	0,6	0,75
Phosphore	0	1,2	1,0
Calcium	0	1,25	0
Chlorure	80	115,9	122

PARAMÈTRES INITIAUX EN FONCTION DU POIDS PATIENT	POIDS	DÉBIT SANG	DOSE CITRATE*	DÉBIT POST-DILUTION	COMPENSATION CALCIUM
	50-60 kg	120 ml/min	3,0 mmol/l	1200 ml/h	120%
	60-70 kg	140 ml/min	3,0 mmol/l	1400 ml/h	120%
	70-80 kg	160 ml/min	3,0 mmol/l	1600 ml/h	120%
	> 90 kg	170 ml/min	3,0 mmol/l	1900 ml/h	120%

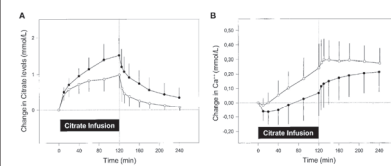
Accumulation de citrate: facteurs de risque



A major contra-indication for the use of citrate anticoagulation is severely impaired liver function or shock with muscle hypoperfusion, both representing a risk of citrate accumulation.

Citrate pharmacokinetics and metabolism in cirrhotic and noncirrhotic critically ill patients

Infusion de citrate à la dose de 0,5 mmol/kg/h pendant 2 heures



→ Clearance du citrate diminuée de moitié

→ Les tests usuels explorant la fonction hépatique n'étaient pas prédictifs d'un métabolisme altéré

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

Cohorte prospective: 133 patients classés selon atteinte hépatique définie par le taux de bilirubine

3% de syndrome d'accumulation en citrate

Pas d'augmentation du taux d'accumulation chez les patients avec atteinte hépatique

Table 4 Acid-base status at start of RCA/CVVHD treatment and end of observation

	Normal liver function (bilirubin <2 mg/dl)		Mild liver failure (bilirubin 2-7 mg/dl)		Severe liver failure (bilirubin >7 mg/dl)	
	Start	End	Start	End	Start	End
Arterial pH	7.33 ± 0.10	7.41 ± 0.06	7.33 ± 0.10	7.44 ± 0.05	7.35 ± 0.10	7.42 ± 0.05
Arterial serum bicarbonate (mmol/L)	20.9 ± 4.8	25.2 ± 2.4	20.5 ± 5.2	25.8 ± 2.0	20.8 ± 4.3	24.7 ± 2.7
Base excess (mmol/L)	-4.1 ± 5.8	1.3 ± 3.2	-4.6 ± 6.3	1.4 ± 6.8	-3.9 ± 5.0	-0.9 ± 6.8
Arterial lactate (mmol/L)	2.27 ± 3.61	1.71 ± 2.22	3.78 ± 4.53	2.63 ± 3.25	2.81 ± 2.69	3.41 ± 4.93
Arterial pCO ₂ (mmHg)	101 ± 34	96 ± 29	99 ± 31	92 ± 28	93 ± 27	96 ± 21
Arterial pCO ₂ (mmHg)	40 ± 11	41 ± 9	41 ± 11	43 ± 8	39 ± 11	39 ± 7

pCO₂, carbon dioxide pressure; pO₂, oxygen pressure. RCA-CVVHD regional citrate anticoagulation and continuous venovenous hemodialysis. Mean ± standard deviation.

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

Table 2 Metabolic characteristic of patients with citrate accumulation

	Before initiation of RCA-CVVHD, mean (95% CI)	At time of diagnosis of citrate accumulation, mean (95% CI)	P value
pH	7.31 (7.27-7.35)	7.20 (7.16-7.24)	<.001
S-bicarbonate, mmol/L	20.2 (18.5-22.0)	14.8 (13.7-15.8)	<.001
iCa, mmol/L	1.14 (1.10-1.18)	1.01 (0.97-1.05)	<.001
tCa, mmol/L	2.13 (1.99-2.27)	2.55 (2.29-2.72)	<.001
tCa/iCa ratio	1.87 (1.79-1.94)	2.51 (2.29-2.82)	<.001
Anion gap, mmol/L	11.0 (8.5-13.5)	15.4 (13.6-17.1)	.003
pO ₂ , mm Hg	104 (89-119)	103 (93-113)	.938
Lactate, mmol/L	7.74 (5.14-10.32)	15.0 (12.72-17.36)	<.001
Bilirubin, mmol/dL	4.65 (2.00-7.29)	8.28 (4.62-11.92)	.104
AST, U/L	690 (195-1184)	3042 (1280-4196)	.001
ALT, U/L	193 (89-296)	1205 (691-1718)	<.001
CGT, U/L	142 (66-218)	83 (56-110)	.079
Thrombocytes	134 (99-169)	97 (73-121)	.075
INR	2.21 (1.96-2.56)	2.94 (2.63-3.33)	.002

Data are presented as mean and 95% CI.

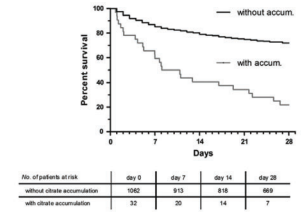


Fig. 2. Survival of the patients with citrate accumulation (gray line) and total cohort of patients treated with CVVHD with regional citrate anticoagulation (black line) after ICU admission. Data are gathered over the years 2008 to 2010; total: 1070 patients, 298 patients died over the period of 28 days after ICU admission; 103 patients were lost to follow up during 28 days and were counted as dead. Log rank, P < .001.

Prédiction de l'accumulation de citrate

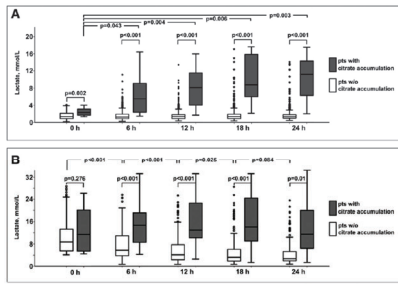
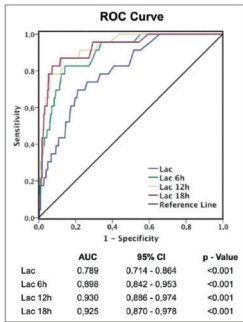
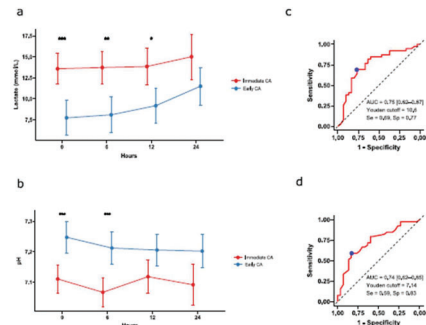


Figure 3. Time course of lactate concentration among the patients with notcritical (A, < 4 mmol/L) and critical (B, ≥ 4 mmol/L) lactate concentration over the first 24 hr of regional citrate anticoagulation (RCA)-continuous veno-venous hemodialysis (CVVHD). The RCA-CVVHD was initiated at time-point 0 hr.

Khadzhynov et al. *Critical care medicine* 2017

Accumulation de citrate : cinétique



Bidar et al. *Critical care medicine* 2025

Durée de vie des filtres et modalité continue

The modality of kidney replacement therapy was significantly associated with filter life span, with :

- CVVHD having the longest filter life span vs CVVH mean difference, 14.68 hours [95%CI, 5.71 to 23.65 hours]; P = .001;
- CVVHD vs CVVHDF: mean difference, 5.14 hours [95%CI, 0.23 to 10.05 hours]; P = .04,
- CVVHDF vs CVVH :mean difference 9.54hours [95% CI, 0.23 to 18.85 hours]; P = .045).

There was no effect on 90-day mortality.

Zarbock et al. *JAMA* 2020

- Vous débutez une EER en CVVHD chez un patient en post-opératoire d'une chirurgie d'endocardite infectieuse. Le patient présente un état de choc avec des besoins en noradrénaline jusque 2 µg/Kg/min.

- Les paramètres d'EER sont les suivants:

Débit sang 90ml/min, débit dialysat 1800 ml/h, Citrate de Na 4% : 3,9 mmol/L de sang, CaCl2 2,4 mmol/L de dialysat; UF nette 0 ml/h

Votre bilan biologique à H12 retrouve :

- pH 7,12 pCO2 39.0 mmHg HCO3- 18 mmol/L lactate 15 mmol/L
- Calcium ionisé 0.9 mmol/L, calcémie totale 2,3 mmol/L
- Na+ 135 mmol/L K+ 4.6 mmol/L Cl- 109 mmol/L HCO3- 17 mmol/L
- Magnésium 0,97 mmol/L Phosphore 1.42mmol/L
- ASAT 3N, ALAT 3N UI/L, Bilirubine tot 100 µmol/L, TP 40%

Que suspectez-vous ? Quelle est votre prise en charge ?

- A/ Il s'agit d'un surdosage en citrate
- B/ Vous arrêtez l'EER en urgence
- C/ Vous arrêtez l'anticoagulation régionale au citrate mais vous poursuivez l'EER
- D/ Une augmentation du débit sang pourrait permettre de corriger la situation
- E/ Le patient ne présente pas de complication métabolique en lien avec l'anticoagulation au citrate

Table 1 Citrate accumulation and alternative diagnoses: summary table

	Citrate accumulation	Citrate net overload	Insufficient trisodium citrate delivery
Mechanism	Incomplete citrate metabolism; persistence of circulating citrate-calcium complexes in the blood	Excess citrate administration relative to buffer requirements	Insufficient alkalotic load administered to the patient to adequately buffer acute kidney injury-associated acidosis
Diagnosis			
Acid-base	Metabolic acidosis	Metabolic alkalosis	Metabolic acidosis
Ca _{ion} /Ca _{total} ratio	Increased (>2.5)	Normal (< 2.5)	Normal (< 2.5)
Other	Increased need for calcium substitution Trend for a decreased ionized calcium level	None	None
Appreciation	Potentially lethal (via severe hypocalcemia)	Benign and easy to fix	Benign and easy to fix
Incidence	Rare	Common	Rare
Management	Decrease blood flow or increase dialysate flow rate (if mild). Consider alternative anticoagulation strategy	Decrease blood flow or increase dialysate flow rate	Increase blood flow or decrease dialysate flow rate

Schneider et al. *Critical Care* (2017) 21:281

Elimination du citrate au cours d'une EER

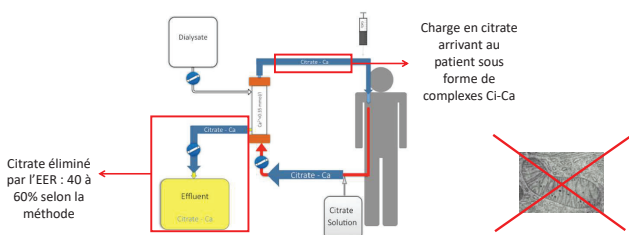


Fig 3 Schematic view of a CRRT circuit with regional citrate administration in CVVH mode. Alternative modes can be used (postdilution CVVH, combined pre- and postdilution CVVH, CVVHD, etc.) according to the protocol used. Citrate solution is administered at the beginning of the CRRT circuit. It forms citrate-calcium complexes, which are largely removed from the blood at the level of the filter. Only complexes which are not removed through the hemofilter return to the patient's blood and need to be metabolized.

- Il faut donc poursuivre l'EER en arrêtant seulement l'anticoagulation régionale au citrate afin d'éliminer les complexes Ci-Ca via l'EER
- Ne surtout pas arrêter complètement l'EER car les capacités de métabolisation du citrate de l'organisme sont dépassées

L'infirmière vous rappelle 4 heures plus tard car décidément rien ne va plus chez cette patiente. La pression artérielle est à 50/20 mmHg malgré des doses de Noradrénaline à 3 µg/Kg/min.

Que faites-vous en urgence ?

Mesure calcémie ionisée patient + administration de chlorure de calcium IV

	Citrate	CC-Ca ²⁺ Dialysate K4 Plus	Multibic 4
Na+	408,00	133,00	140,00
K+		4,00	4,00
Mg2+		1,00	0,50
Ca2+		0,00	1,50
Cl-		117,75	113,00
HCO3-		20,00	35,00
Lactate		0,00	0,00
HPO42-		1,25	0,00
Glucose		5,55	5,55
Citrate3-	136,00	0,00	0,00
pH		7,40	7,40
SiO2		21,25	35,00
SiO2		22,27	35,00
SiO2		-1,00	0,00



Le bain de dialyse d'une anticoagulation au citrate ne contient pas de calcium, en cas d'oubli de changement des bains : hypocalcémie sévère

Vous regardez de plus près le dossier de la patiente de votre collègue. L'EER en est CVVH héparine, la patiente a 60 ans et a été admise en réanimation pour tableau d'angiocholite. Elle a pour antécédents une HTA et un diabète de type 2. La patiente est sous CVVH depuis 48 heures maintenant. Elle est par ailleurs sous oxygénothérapie à 4L/min et sous NORADRENALINE à 0,2 µg/Kg/min. Aucune alimentation n'a pu être reprise.

Le bilan sanguin retrouve les paramètres suivants :

pH 7,28 pCO₂ 32 mmHg paO₂ 80 mmHg HCO₃⁻ 17 mmol/L lactate 1.5 mmol/L Na⁺ 138 mmol/L K⁺ 4 mmol/L Cl⁻ 98 mmol/L glycémie 6 mmol/L

Comment expliquez-vous cette acidose ?

Quel(s) examen(s) demandez-vous ?

PHOXILUM : APRÈS RECONSTITUTION

1000 ml de solution reconstituée contiennent :

Principes actifs	mmol/l	mEq/l
Calcium Ca ²⁺	1,25	2,50
Magnésium Mg ²⁺	0,600	1,20
Sodium Na ⁺	140,0	140,0
Chlorure Cl ⁻	115,9	115,9
Phosphate d'hydrogène HPO ₄ ²⁻	1,20	2,40
Bicarbonate HCO ₃ ⁻	30,0	30,0
Potassium K ⁺	4,00	4,00

La cétonémie est à 2 mmol/L

Comment expliquez-vous le trouble acido-basique ?

Euglycemic ketoacidosis, a common and underrecognized complication of continuous renal replacement therapy using glucose-free solutions

Maxime Coutrot, Guillaume Hékimian, Thibaut Moulin, Nicolas Bréchet, Matthieu Schmidt, Sébastien Besset, Anna Nieszkowska, Guillaume Franchineau, Simon Bourcier, Olivier Bourron, Charles-Edouard Luyt and Alain Combes

Table 1 Biological analysis, glucose intake and insulin infusion in the 18 patients who developed euglycemic ketoacidosis on CRRT using glucose-free replacement solution

	24 h before ketoacidosis detection	At ketoacidosis detection	After glucose and insulin infusion
pH	7.37 (7.31–7.43)	7.36 (7.32–7.39)	7.44 (7.32–7.49)
Bicarbonates level, mmol/l	20.4 (18.1–22.2)	17.3 (14–18.9)	21 (19.1–21.9)
Creatinine, µmol/l	186 (112–232)	135 (98–159)	119 (90–161)
pCO ₂ , mmHg	34.4 (29.7–38)	31.9 (26.9–35)	30 (28.1–38)
Lactate, mmol/l	1.7 (1.3–2)	1.7 (1.3–2)	1.6 (1.3–2.4)
Insulin infusion, IU/h	0.075 (0–1.9)	0 (0–0)	3 (2–5)
Glucose infusion, g/h	1.05 (0.51–1.50)	1.05 (1.05–2.10)	2 (1–12)
Enteral nutrition, kcal/h	0 (0–0)	0 (0–31)	21 (0–62)
Glycemia, mmol/l	6.1 (4.8–7.3)	6.2 (5–7)	6.5 (5–8)
Ketonaemia, mmol/l	Unknown	2 (1.7–3.1)	0 (0–0.025)
Ketones in the effluent liquid, g/l	Unknown	0.15 (0.025–0.8)	0 (0–0)
CRRT glucose removal, g/24 h	51 (45–63)	54 (44–60)	70 (58–73)

CRRT glucose removal was calculated assuming that glucose clearance is equal to ultrafiltration rate, and corrected according to predilution infusion rate [5]

Prescription en pratique

Dose prescrite : 30 mL/Kg/h = effluent total pour objectif de 25 mL/Kg/h reçus

- CVVHD : débit dialysat
- CVVH : débit pré-dilution + post-dilution

Débit sang : abaque correspondant entre débit sang et effluent pour

- Optimiser dose de citrate si ARC
- Limiter la fraction de filtration en hémofiltration

Citrate : asservi au débit sang

ATTENTION NE PAS MODIFIER LE DEBIT SANG DE MANIÈRE ARBITRAIRE NOTAMMENT EN EER AU CITRATE

- Pas d'augmentation de l'efficacité
- Risque d'apports en citrate trop importants

UF nette : selon profil hémodynamique du patient

Quelle modalité ?

Continue / Intermittente ?

Mécanisme d'épuration ?
Membrane ?

Mortalité ?

Récupération rénale ?

Optimisation de l'administration de l'EER

UF nette ?

Dose ?

Anticoagulation ?



EDITORIAL

The artificial kidney induces AKI? Not if we apply "kidney-protective" renal replacement therapy

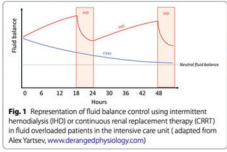


Fig. 1 Representation of fluid balance control using intermittent hemodialysis (IHD) or continuous renal replacement therapy (CRRT) in fluid overloaded patients in the intensive care unit (adapted from Alex Yartsev, www.derangedphysiology.com)

RRT remains the key treatment of both the metabolic and fluid overload consequences of severe AKI, in particular in the context of multi-organ dysfunction. To provide safe and effective RRT we need to apply "kidney-protective" therapy as much as possible to limit any perceived harm.

Legrand et al. ICM 2019

Conclusion

- La prescription de l'EER doit être adaptée au patient
- De nombreux paramètres au-delà du « simple » choix de lu mécanisme d'épuration doivent être pris en considération
- Pas de supériorité démontrée sur mortalité d'un type de mécanisme d'épuration en réanimation
- Choix de la modalité selon profil hémodynamique
- Nécessité de bien connaître les solutés utilisés dans sa réanimation
- Personnalisation de la prescription pour chaque patient et au cours du temps pour un même patient
- Dépend des ressources locales : machines disponibles, formation des équipes