Epuration extra-rénale au cours des insuffisances rénales aiguës

Quand débuter? Quelles techniques? Quelles cibles?

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Epuration extra-rénale en soins critiques?

- **Des bénéfices attendus**
  - Thérapeutiques (K+, acidose, toxines urémiques, toxiques)
  - Préventif (surcharge hydrosodée et ses complications)
- **Des risques pouvant (parfois) être anticipés / prévenus**
  - Instabilité hémodynamique
    - Lésions rénales secondaires
    - Ischémie myocardique…
  - Allergie à la membrane
  - PK/PD (antibiotiques…)
  - Cathéter

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EER et IRA : spécificités

Une récupération est possible dans les heures suivants la prise en charge

- **Urgence métabolique ou volémique?**
  - Heures ? Jours?
- **Amélioration attendue?**
  - Heures? Jours?
- **Risques liés à l'EER?**
  - Faibles? Elevés?

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EER et IRA : spécificités

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  - Heures? Jours?
- **Risques liés à l'EER?**
  - Faibles? Elevés?

- **Un traitement médical est-il possible?**
- Une épuration peut elle être rapidement disponible si l'EER est retardée?
- Une chirurgie / un examen sont-ils prévus dans les prochaines heures?

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Pourquoi débuter une épuration extra-rénale?

5

Indications d'EER immédiate

- Indications thérapeutiques

Table 1 Traditional triggers to initiate dialysis in patients with acute kidney injury

Indications	Triggers to initiate dialysis
Clinical	Refractory pulmonary edema
	Oligoanuria
	Pericarditis
	Uremic encephalopathy
Laboratory	Refractory hyperkalemia
	BUN ≥100 mg/dL (urea ≥30 mmol/L)
	Refractory metabolic acidosis (pH < 7.2)
	Refractory electrolyte abnormalities
	Tumor lysis syndrome (hyperuricemia and hyperphosphatemia)
	Metabolic coma (urea cycle defects, hyperammonemia)
	Some specific cases of severe poisoning/drug over dosage

Davenport et al. Hemodial Int 2015

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Indications d'EER immédiate

- Indications thérapeutiques

Données fixes vs. Dynamiques?

Table 1 Traditional triggers to initiate dialysis in patients with acute kidney injury

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	Pericarditis
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	Metabolic coma (urea cycle defects, hyperammonemia)
	● Some specific cases of severe poisoning/drug over dosage

Davenport et al. Hemodial Int 2015

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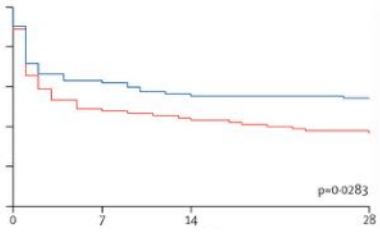
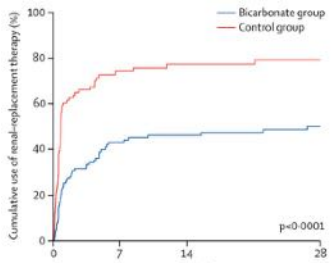
Peut on moduler ces indications?

Sodium bicarbonate therapy for patients with severe metabolic acidaemia in the intensive care unit (BICAR-ICU): a multicentre, open-label, randomised controlled, phase 3 trial

Survie (sous groupe AKI KDIGO 2-3)



Incidence cumulée EER



Traitement médical de l'acidose métabolique sévère: **meilleure survie et <u>moindre recours à l'EER</u>**

Jaber et al. Lancet 2018

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EER et IRA : spécificités

- **Indications « préventives »**
    1. Prévention surcharge hydrosodée

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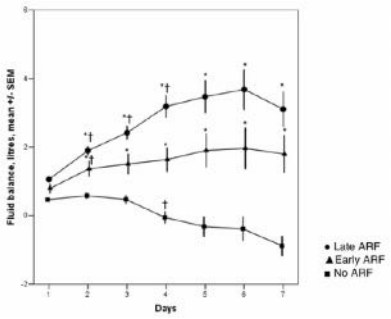
Balance des fluides et survie

Research

Open Access

A positive fluid balance is associated with a worse outcome in patients with acute renal failure



- Association IRA - surcharge hydrosodée
- Association surcharge hydrosodée - mortalité

Mean daily fluid balance among 60-day survivors and non-survivors with acute renal failure (ARF), stratified by time of onset

Mean fluid balance, L/24 hours	Survivors	Non-survivors	*P* value
ARF	0.15 ± 1.06	0.98 ± 1.50	<0.001
Early ARF (occurring within 2 days of ICU admission)	0.14 ± 1.05	1.19 ± 1.48	<0.001
Late ARF (occurring more than 2 days after ICU admission)	0.11 ± 1.03	0.39 ± 1.40	0.06

Payen et al. Crit Care, 2008

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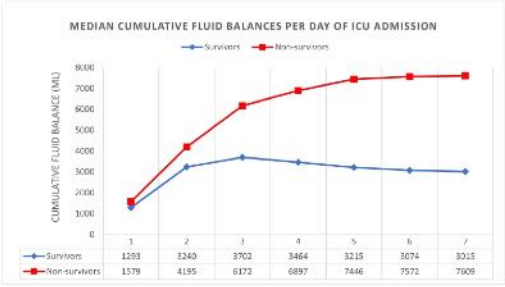
Balance des fluides et durée de ventilation mécanique

RESEARCH ARTICLE

Cumulative fluid balance predicts mortality and increases time on mechanical ventilation in ARDS patients: An observational cohort study

- *Une balance positive est associée à une durée de ventilation mécanique et une mortalité plus importante*



	Group I <0 l. N = 123	Group II 0–3.5 l. N = 177	Group III 3.5–8l. N = 151	Group IV ≥8 l. N = 149	P-value
Mortality–n (%)					
28–day mortality	11 (8.9)[II,III,IV]	34 (19.2)[I, IV]	40 (26.5)[I, IV]	71 (47.7)[I,II,III]	*<0.001*
90-day mortality	16 (13.0)[II,III,IV]	50 (28.2)[I, IV]	52 (34.4)[I, IV]	84 (56.4)[I,II,III]	*<0.001*
ICU mortality	5 (4.1)[III, IV]	15 (8.5)[III, IV]	33 (21.9)[I, II, IV]	57 (38.3)[I, II, III]	*<0.001*
Ventilation					
Ventilator–free days on day 28	25.1 [20.8–26.6][II, III, IV]	24.3 [10.4–26.0][I, III, IV]	19.2 [0.00–25.1][I, II, IV]	0.00 [0.00–19.5][I, II, III]	*<0.001*
Weaned off ventilator by day 28	107 (87.0)[III, IV]	139 (78.5)[IV]	106 (70.2)[I, IV]	70 (47.0)[I, II, III]	*<0.001*
Duration of mechanical ventilation–hours	62.0 [31.5–136][III, IV]	80.0 [39.0–136][III, IV]	132 [61.0–257][I, II, IV]	189 [101–358][I, II, III]	*<0.001*
Length of stay–days					
ICU length of stay	5.03 [3.05–8.65][III, IV]	5.45 [3.49–8.32][III, IV]	8.39 [4.65–12.8][I, IV]	11.6 [6.35–20.7][I, II, III]	*<0.001*
Hospital length of stay	17.0 [10.0–32.5][IV]	15.0 [9.00–35.0][IV]	21.0 [12.0–38.0]	28.5 [14.0–45.0][I, II]	*0.004*

Van Mourik et al. PLoS One, 2019

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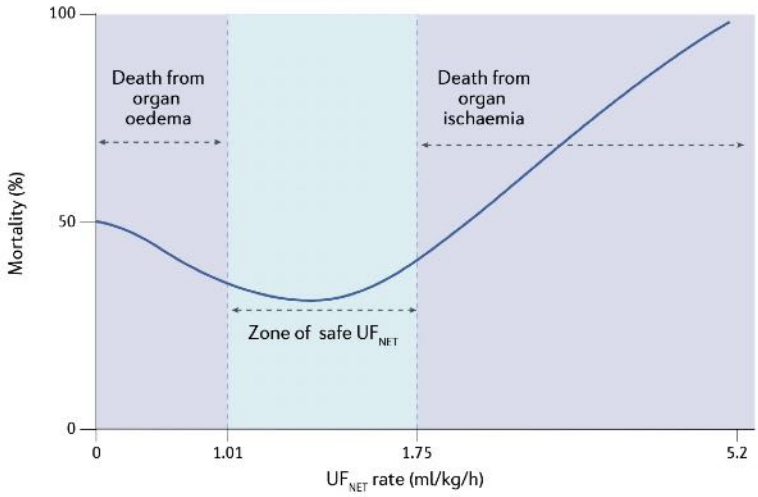
Ultrafiltration trop élevée : quels risques?



- Limiter les apports quotidiens…

Murugan et al. Nature Rev Nephrol 2021

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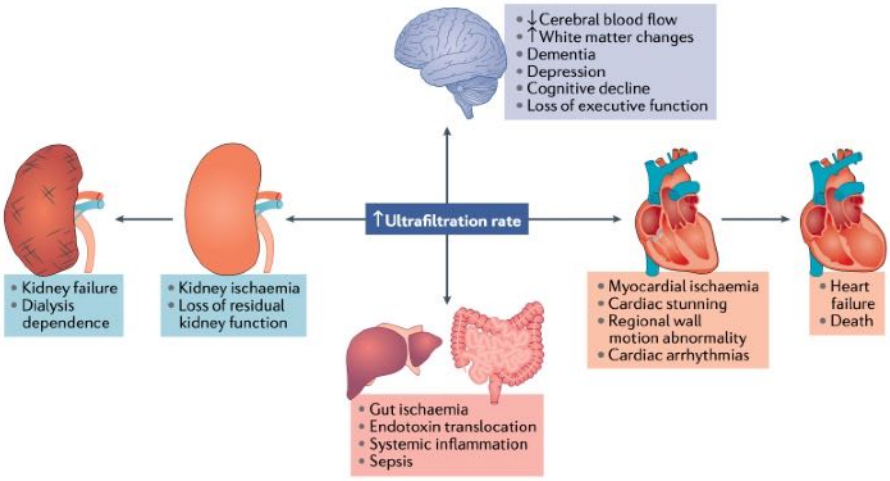
Ultrafiltration trop élevée : quels risques?



Murugan et al. Nature Rev Nephrol 2021

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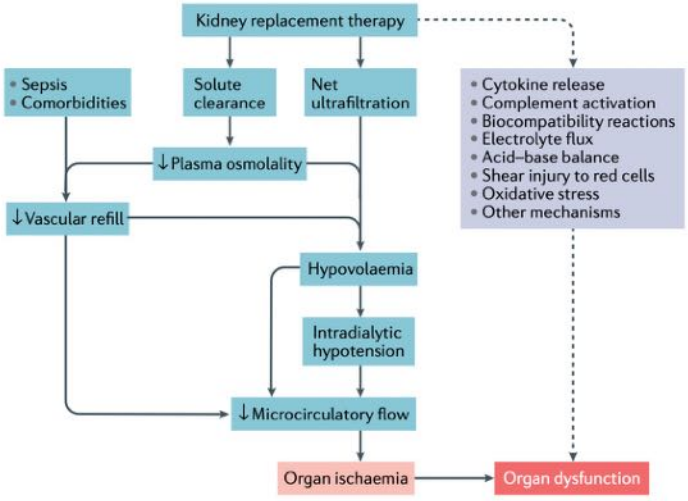
Ultrafiltration et EER: quels risques en situation critique?



- **Estimer les capacités de refilling / tolérance HD**
  - Tonus vasomoteur, inotropisme, activité chronotrope
  - Hypoalbuminémie, dyskaliémie
  - Sepsis en cours
  - Sédation / vasoplégiques
- **Caractère délétère d'une UF « forcée »**
  - Viser une balance hydrique quotidienne nulle (à négative) dès la stabilisation hémodynamique obtenue
  - S'adapter aux apports quotidien et au évolutions hémodynamiques

Murugan et al. Nature Rev Nephrol 2021

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EER et IRA : spécificités

- **Indications « préventives »**
  1. Prévention surcharge hydrosodée
     a. Réduction durée de ventilation mécanique
     b. Réduction mortalité
  2. Réduction du besoin d'ultrafiltration de haut volume
     a. Réduction des hypotensions per-dialytiques
  3. Prévention hypertension artérielle sévère
     a. Réduction risque vasculaire
     - ➢ **Savoir anticiper les problématiques**

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Quand débuter une épuration extra-rénale?

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EER précoce vs. tardive: de multiples définitions et endpoints

Author	Year	RRT	Nos.	Early	Later	Mortality
Retrospective						
do Nascimento[2]	2012	PD and HD	86	BUN <75	BUN >75	39% vs. 69%*
Shiao[16]	2009	CRRT and HD	98	O/R	I/F	43% vs. 75%*
Oh[17]	2012	CRRT	210	<2 days[a]	<2 days[a]	66% vs. 86%*
Leite[18]	2013	HD and PIRRT	150	F <24 h[b]	F >24 h[b]	52% vs. 78%*
Wu[19]	2012	CRRT	71	R	I/F	50% vs. 85%*
Elahi[20]	2004	CRRT	64	UO <100 mL/h	Urea ≥30	43% vs. 23%*
Ji[21]	2011	CRRT	58	UO < 100 mL/h for <12 h	UO <100 mL/h for >12 h	9% vs. 38%*
Piccinini[22]	2006	CRRT	80	Sepsis <12 h in ICU	Sepsis traditional	54% vs. 61%*
Liu[23]	2006	HD and CRRT	243	BUN <76	BUN >76	61% vs. 80%*
Bagshaw[24]	2009	HD and CRRT	1238	Cr <309	Cr >309	53% vs. 71%*
Payen[25]	2008	HD and CCRT	278	<48 h in ICU	>48 h ICU	45% vs. 65%*
Iyem[26]	2009	CRRT	185	UO <0.5 mL/kg/h and 50% ↑ urea and creatinine	>48 h UO 0.5 mL/kg/h and 50% ↑ urea and creatinine	5% vs. 7%
Carl[27]	2010	CRRT	147	BUN <66	BUN >100	52% vs. 68%
Chou[28]	2011	CRRT and PIRRT	370	O/R	I/F	71% vs. 70%
Shum[29]	2013	CRRT	120	R	F	48% vs. 48%
Jun[30]	2014	CRRT	439	<7.1 h[b]	>46 h[b]	36% vs. 40%
Prospective						
Lim[31]	2015	CRRT	140	R/I	Traditional	50% vs. 34%

Davenport A. Hemodial Int 2015

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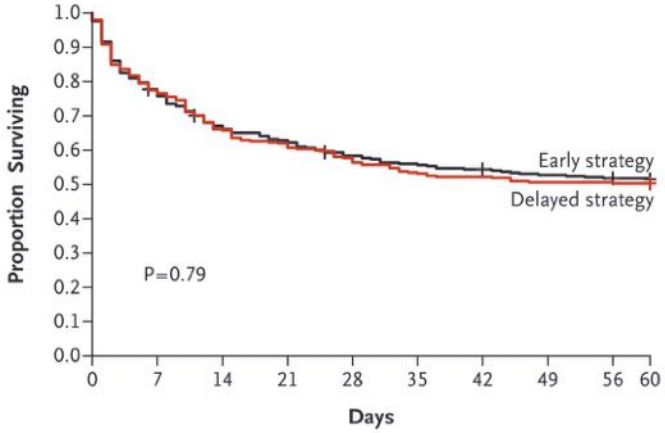
EER précoce vs. tardive

Précoce
- AKI stade 3

Tardif
- Oligo-anurie > 72h
- Urée > 40 mmol/L
- K >6 ou >5 malgré ttt
- pH < 7.15 malgré ttt
- OAP

ORIGINAL ARTICLE

Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit



Gaudry et al. NEJM 2016

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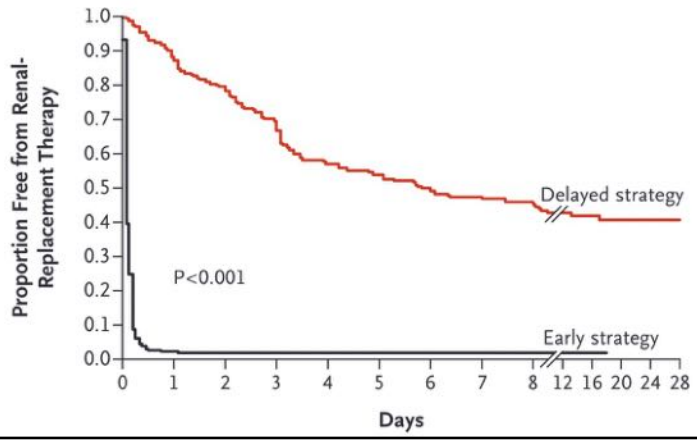
EER précoce vs. tardive

ORIGINAL ARTICLE

Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit



Gaudry et al. NEJM 2016

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EER tardive vs. très tardive

Comparison of two delayed strategies for renal replacement therapy initiation for severe acute kidney injury (AKIKI 2): a multicentre, open-label, randomised, controlled trial

	Univariable analysis		Multivariable analysis	
	Hazard ratio (95% CI)	p value	Hazard ratio (95% CI)	p value
More-delayed strategy	1·34 (0·96–1·89)	0·13	1·65 (1·09–2·50)	0·018
Simplified Acute Physiology Score III	1·03 (1·02–1·05)	<0·0001	1·03 (1·01–1·05)	0·0005
Mechanical ventilation	2·90 (1·47–5·70)	<0·0001	3·44 (1·52–7·81)	0·0020
Catecholamine infusion	1·69 (1·17–2·44)	0·0080	1·13 (0·69–1·84)	0·64
Sepsis status	..	0·064	..	0·19
Sepsis	0·78 (0·47–1·30)	..	0·56 (0·28–1·12)	..
Septic shock	1·44 (0·98–2·12)	..	0·91 (0·51–1·64)	..
Time between ICU admission and acute kidney injury	0·69 (0·36–1·31)	0·24	0·70 (0·31–1·59)	0·39

ICU=intensive care unit.

Gaudry et al. Lancet 2021

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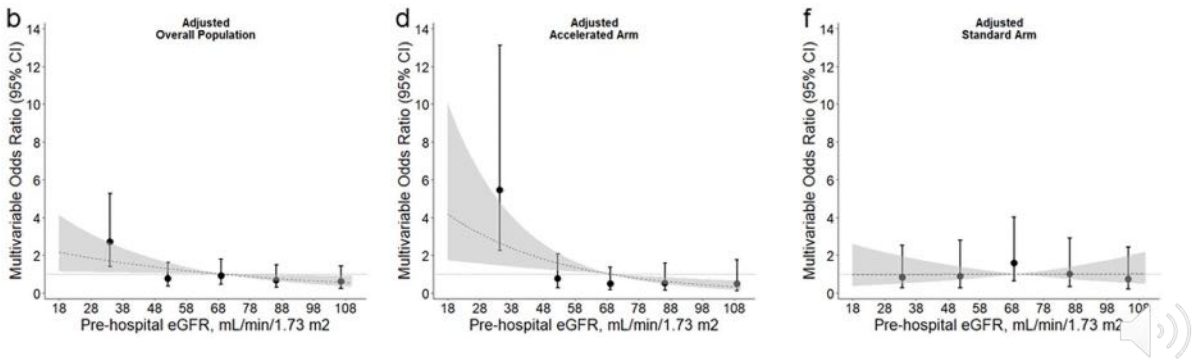
eGFR basal et délai d'introduction EER

ORIGINAL

Impact of renal-replacement therapy strategies on outcomes for patients with chronic kidney disease: a secondary analysis of the STARRT-AKI trial

- Survie identique
- Dépendance dialyse à J90 : bras accéléré et DFG bas
  - ➢ **En particulier observée si CKD 3-4**



Gaudry et al. Lancet 2021

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EER introduction précoce vs. tardive

- **Résultats études AKIKI, IDEAL-ICU et STAART-AKI concordants**
- L'introduction d'une EER en réanimation doit être basée sur
  - *Des critères de mauvaise tolérance*
    - K > 6 mmol/L, pH < 7.2 ou HCO3 < 12 mmol/L
    - OAP
  - *La persistance d'une IRA sévère*
    - Oligo-anurie > 72 h
    - Urée > 40 mmol/L

➢ **Une dialyse « retardée » (spontanément ou grâce à un traitement médical) permet aussi de débuter une EER dans des conditions hémodynamiques plus favorables.**

Gaudry et al. NEJM 2016, Barbar et al. NEJM 2018, STAART-AKI. NEJM 2020

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Un transfert en clinique à mettre en pratique… de manière raisonnée

- **Situations à risque de troubles métaboliques très rapides**
  - Rhabdomyolyse et syndrome de lyse tumorale
    - EER probablement plus rapide
- **Besoin d'ultrafiltration / décongestion et non d'épuration (UF)**
  - Syndrome cardio-rénal
  - Post-opératoire de chirurgie cardiaque
    - UF isolée / EER plus rapide

Zarbock et al. JAMA 2016
(ELAIN study)

- **Hémodialysés chronique**
  - EER plus rapide (pas d'amélioration attendue)
- **Cirrhotique**
  - Elévation plus lente de la créatininémie

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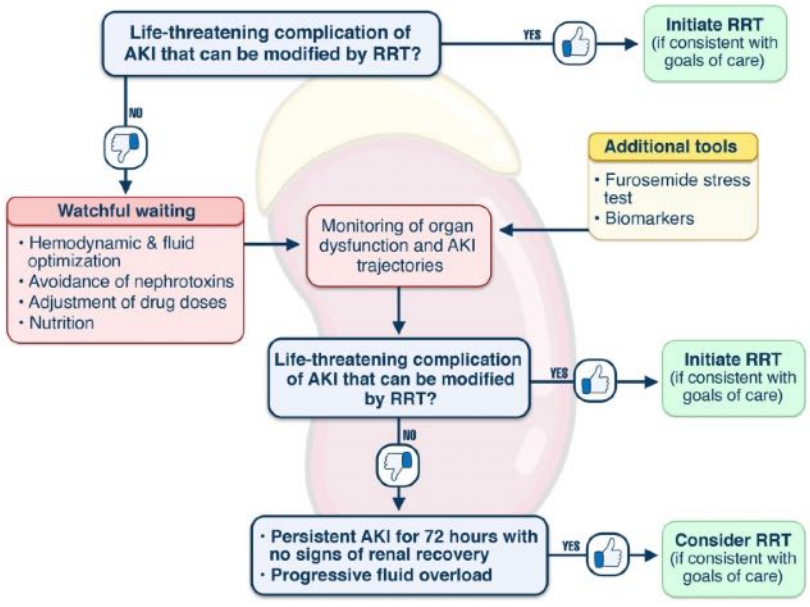
Un transfert en clinique à mettre en pratique… de manière raisonnée



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Quelle technique utiliser?

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Modalités d'EER – IRA: l'éternel débat

Characteristic	RRT modality			
	IHD	SLED	CRRT	PD
Treatment duration (h)	3–6	6–18	24	24
Frequency	3 times per week plus additional treatments as indicated	3 times per week plus additional treatments as indicated	Daily	Daily
Mode of solute transport	Diffusion/convection/both	Diffusion/convection/both	Diffusion/convection/both	Diffusion
Blood flow (ml/min)	200–350	100–300	100–250	N/A
Dialysate flow (ml/min)	300–800	100–300	0–50	N/A
Filter size (m^2)	1.7–2	0.4–1.7	0.6–1.5	N/A
Urea clearance (ml/min)	150–180	90–140	20–45	15–35
Need for anticoagulation	Can be readily delivered without anticoagulation	Can be readily delivered without anticoagulation	Generally required	No

Wald et al. ICM 2022

Supériorité <u>théorique</u> en faveur des techniques continues

- Chez un patient instable sur le plan hémodynamique, l'UF horaire plus faible et la réduction plus lente de l'urée (osmole) pourrait favoriser la tolérance HD
  - Mais un patient instable doit il bénéficier d'UF…?
  - En l'absence d'UF, une EER est elle nécessaire en urgence?

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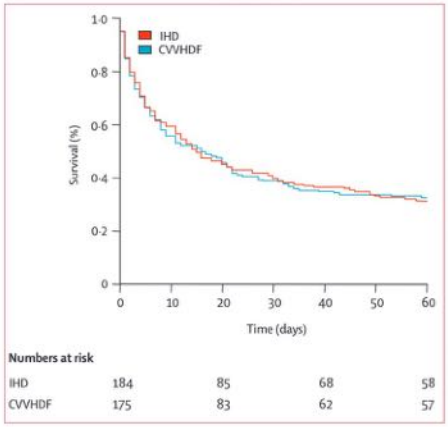
Modalités d'EER – IRA: l'éternel débat

Continuous venovenous haemodiafiltration versus intermittent haemodialysis for acute renal failure in patients with multiple-organ dysfunction syndrome: a multicentre randomised trial



	Intermittent haemodialysis (n=184)	Continuous venovenous haemofiltration (n=175)	p value
Hypotension*	72 (39%)	61 (35%)	0·47
Bleeding event†	13 (7%)	12 (7%)	0·89
Thrombocytopenia	22 (12%)	31 (18%)	0·12
Hypoglycaemia	12 (7%)	7 (4%)	0·42
Hypophosphataemia	13 (7%)	14 (8%)	0·71
Hypothermia	10 (5%)	31 (17%)	0·0005
Arrhythmia	18 (10%)	9 (5%)	0·15
Catheter infection	2 (1%)	3 (2%)	0·95

Vinsonneau et al. Lancet 2006

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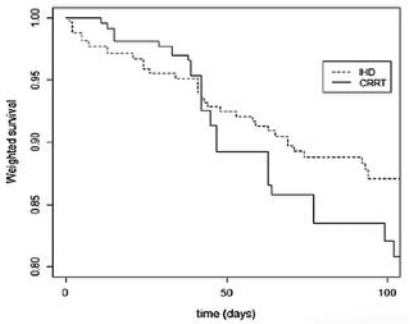
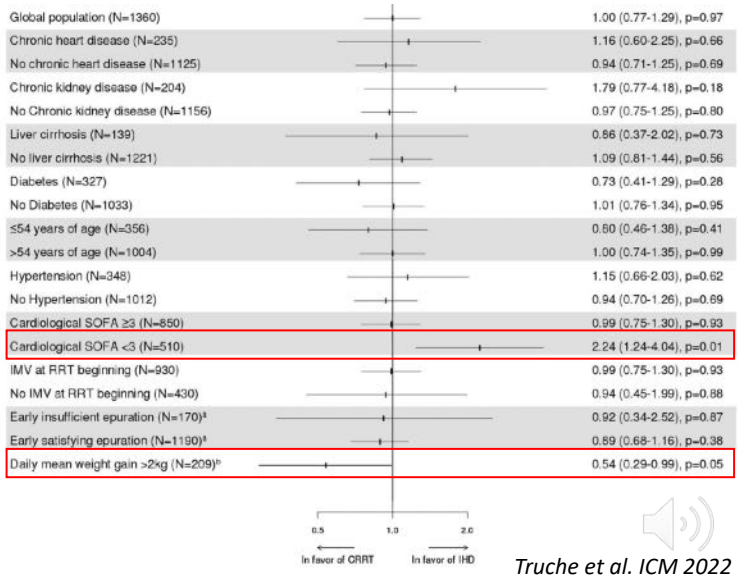
Modalités d'EER – IRA: l'éternel débat

Continuous renal replacement therapy versus intermittent hemodialysis in intensive care patients: impact on mortality and renal recovery





Truche et al. ICM 2022

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Quand privilégier une technique continue?

Comparing Renal Replacement Therapy Modalities in Critically Ill Patients With Acute Kidney Injury: A Systematic Review and Network Meta-Analysis

Comparison	Direct Estimate (95% CI); Certainty of Evidence	Indirect Estimate (95% CI); Certainty of Evidence	Network Estimate (95% CI); Certainty of Evidence[a]	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,c]	There may be no important difference
CRRT vs PD	1.08 (0.76–1.49); low[a,b]; 3 studies	1.28 (0.90–1.82); moderate[a]	1.16 (0.92–1.49); low[a,c]	CRRT may increase mortality compared with PD
CRRT vs SLED	1.12 (0.85–1.47); moderate[a]; 5 studies	0.94 (0.63–1.41); low[a,b]	1.06 (0.85–1.33); low[a,c]	CRRT may increase mortality compared with SLED
IHD vs PD	NA	1.12 (0.85–1.46); low[a,b]	1.12 (0.85–1.46); very low[a,b,c]	Whether there is an important difference or not is very uncertain
IHD vs SLED	NA	1.02 (0.79–1.31); moderate[a]	1.02 (0.79–1.31); low[a,c]	There may be no important difference
PD vs SLED	0.88 (0.71–1.10); moderate[a]; 2 studies	1.05 (0.68–1.62); low[a,b]	0.91 (0.75–1.11); low[a,c]	PD may reduce mortality compared with SLED

Mortalité similaire

Ye et al. Crit Care Explo 2021

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Faut-il privilégier une technique d'EER?

Comparing Renal Replacement Therapy Modalities in Critically Ill Patients With Acute Kidney Injury: A Systematic Review and Network Meta-Analysis

Comparison	Direct Estimate (95% CI); Certainty of Evidence	Indirect Estimate (95% CI); Certainty of Evidence	Network Estimate (95% CI); Certainty of Evidence[a]	Plain Text Summary
CRRT vs IHD	1.15 (0.91–1.44); moderate[b]; 7 studies	NA	1.15 (0.91–1.45); low[b,c]	CRRT may increase RRR compared with IHD
CRRT vs PD	0.97 (0.60–1.55); moderate[a]; 2 studies	0.71 (0.38–1.35); moderate[a]	0.87 (0.60–1.27); low[a,c]	CRRT may reduce RRR compared with PD
CRRT vs SLED	0.84 (0.60–1.16); moderate[a]; 4 studies	1.13 (0.55–2.34); moderate[a]	0.88 (0.65–1.19); low[a,c]	CRRT may reduce RRR compared with SLED
IHD vs PD	NA	0.76 (0.49–1.18); moderate[a]	0.76 (0.49–1.18); low[a,c]	IHD may reduce RRR compared with PD
IHD vs SLED	NA	0.77 (0.53–1.12); moderate[a]	0.77 (0.53–1.12); low[a,c]	IHD may reduce RRR compared with SLED
PD vs SLED	1.18 (0.68–2.04); moderate[b]; 2 studies	0.87 (0.49–1.54); moderate[a]	1.02 (0.68–1.51); low[b,c]	There may be no important difference

Récupération rénale similaire

Ye et al. Crit Care Explo 2021

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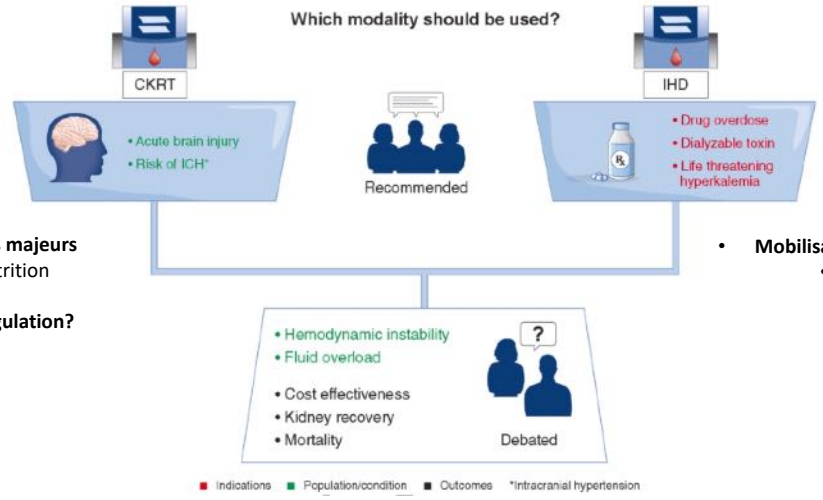
Quand privilégier une technique particulière?



- **Apports quotidiens majeurs**
  - PFC, nutrition
- **Troubles de la coagulation?**
  - Citrate
- **Mobilisations / réhabilitation**
  - Kiné, chirurgies

Chaibi et al. cJASN 2023

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Approche pragmatique

- **Si CVVHD/F utilisée en 1ère ligne**
  - Savoir stopper l'épuration / l'ultrafiltration pour mieux estimer la reprise de fonction
  - Adapter les doses de traitements (antibiotiques…)
- **Si HDI uniquement disponible: s'adapter aux besoins / risques propres du patient**
  - Séances longues si nécessaire (voir SLEDD)
  - Alternance avec UF isolée
  - Séances quotidiennes si nécessaire
- **Alternance des techniques si les cibles thérapeutiques ne sont pas atteintes**

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Quand privilégier une technique particulière?

- **Débat biaisé**
  - Fonction de la disponibilité des techniques (coûts, boucle d'eau, expertise, surveillance…)
- **Unité disposant des 2 techniques**
  - Utilisation combinée selon l'évolution du patient: relais CVVH(D)F > HDI
  - Expertise néphrologique/ expérience
- **HDI**
  - Mono-défaillance rénale = standard en unité de Néphrologie

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Quelle dose de dialyse?

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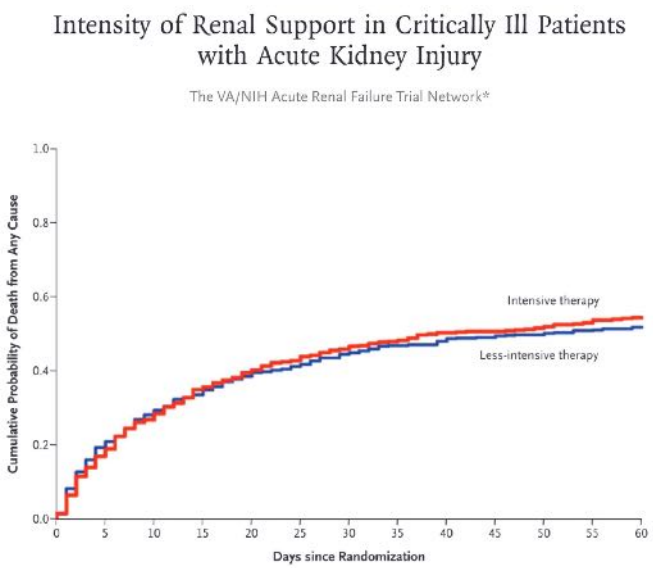
Intensive vs. less-intensive therapy (mixed techniques)

CVVH 35 mL/kg/h
ou HD/SLEDD 6/sem

Vs.

CVVH 25 mL/kg/h
ou HD/SLEDD 3/sem



VA/NIH NEJM 2008

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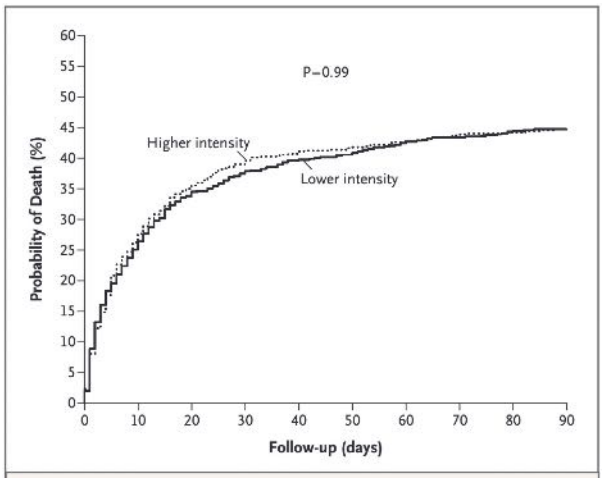
Intensive vs. less-intensive therapy (CVVHDF only)

CVVHDF 40 mL/kg/h

Vs.

CVVHDF 25 mL/kg/h



RENAL NEJM 2009

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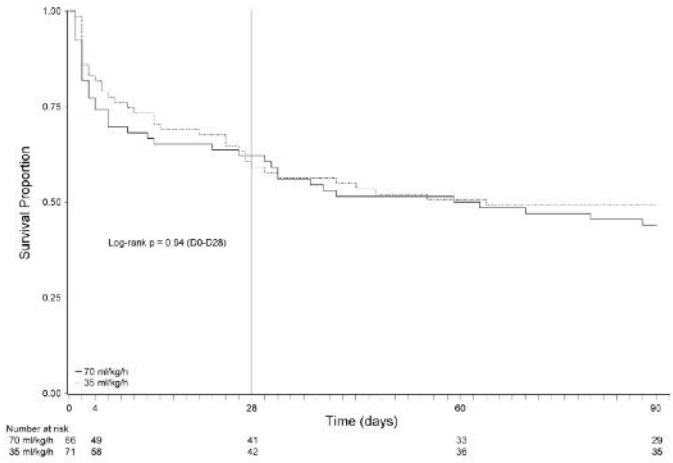
Intensive vs. less-intensive therapy (sepsis)

High-volume vs. Standard-volume haemofiltration for septic shock patients with acute kidney injury (IVOIRE study): a multicentre randomized controlled trial

CVVHF 70 mL/kg/h

Vs.

CVVHF 35 mL/kg/h



Joannes-Boyau et al. ICM 2013

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Est-ce la bonne question?

could yield similarly acceptable outcomes. Moreover, adequacy in the setting of acute RRT extends well beyond urea clearance and is also reflected by other dimensions including achievement of electrolyte and acid–base homeostasis. In addition, close attention needs to be paid to the unintended consequences of blood purification, namely removal of vital medications, the depletion of essential vitamins and trace elements and excessive clearance of key electrolytes (e.g., phosphate).

- Kt/V peu applicable en réanimation / IRA. Dialysance ionique?

➢ **Le nombre de séances / durée des séances doivent prendre en considération l'ensemble des besoins pouvant être modulés par l'EER** (urée, K+, surcharge hydrosodée, disponibilités, anticoagulation…)

Wald et al. ICM 2022

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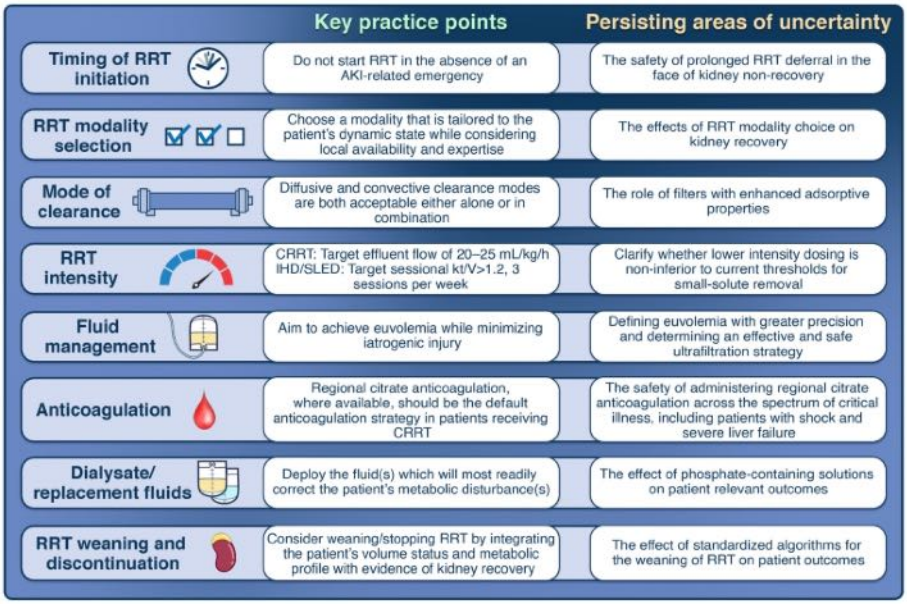
Synthèse et perspectives



Wald et al. ICM 2022

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Conclusions

- « In the absence of evidence of clinical superiority of one KRT modality, the choice must be addressed not only in terms of clinical outcomes, but also ressources and logistics.
- Pending results of new RCTs taking recent knowledge on KRT initiation and management into account, the choice should be guided mainly by organizational considerations in each unit and without condemning any modality in the absence of proof.»

Chaibi et al. cJASN 2023

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