

IRA aux soins intensifs: CRRT vs IRRT

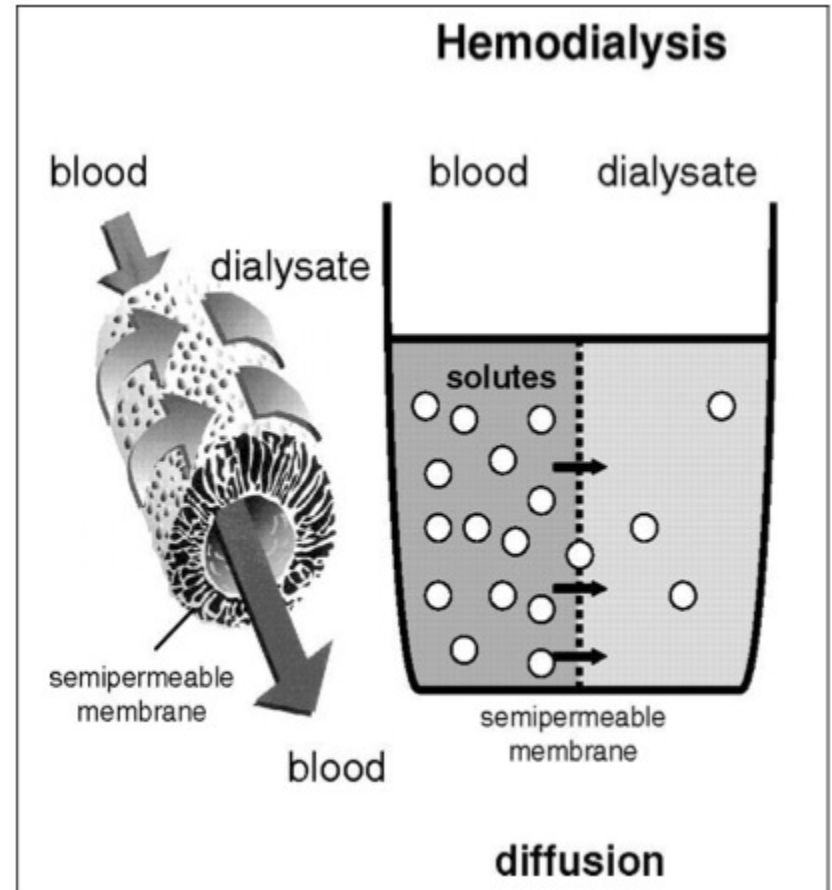
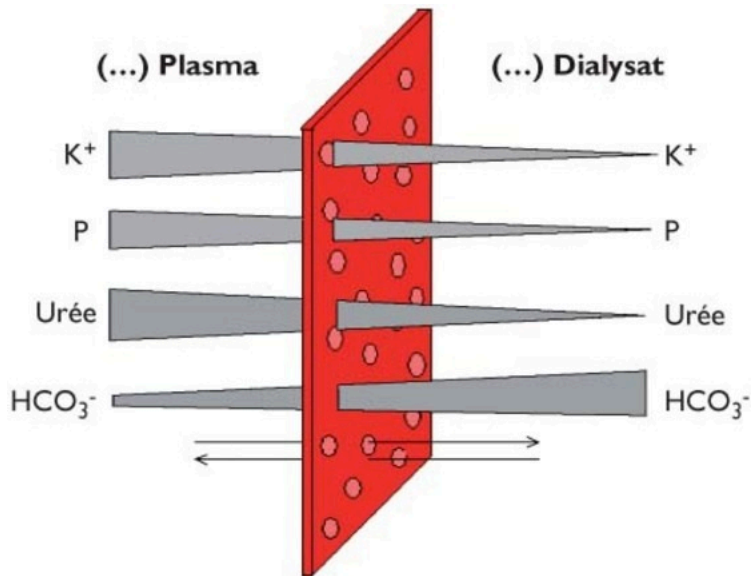
Journal club 10 avril 2014

Epuration extra-rénale

RAPPELS

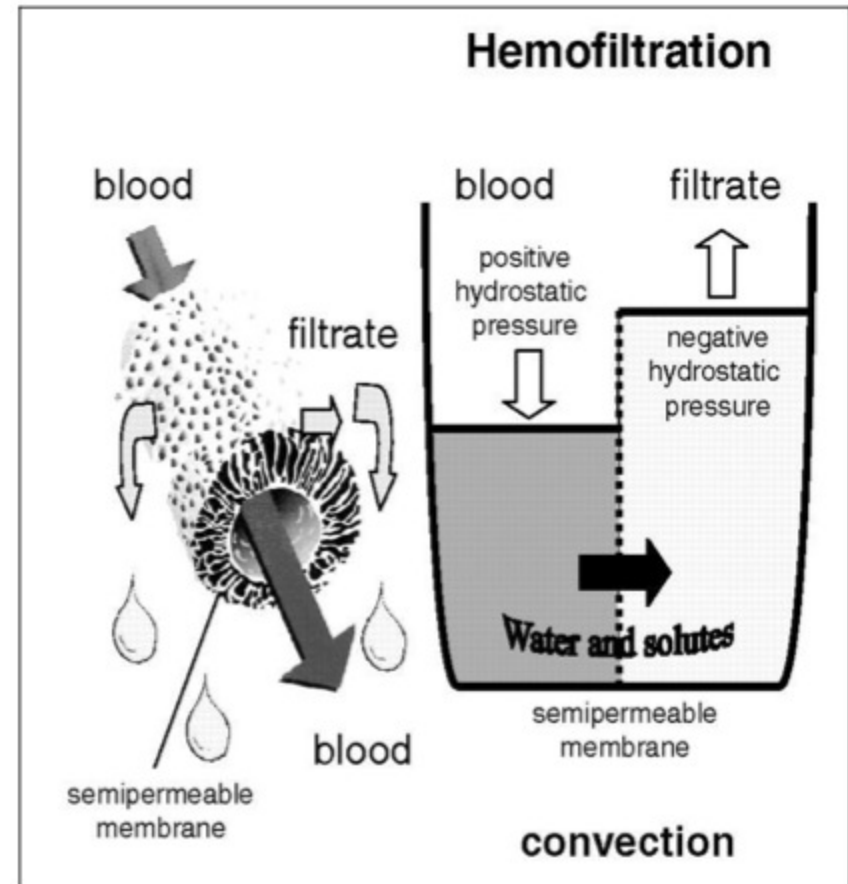
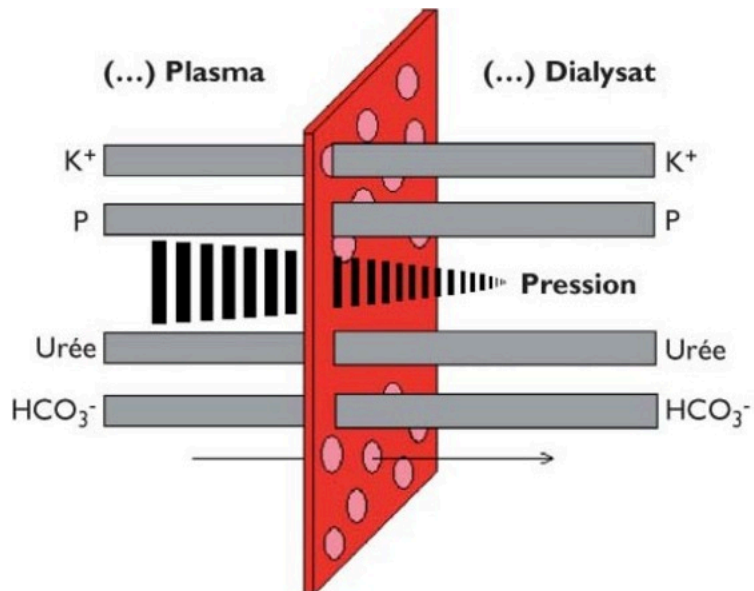
Hémodialyse

- Diffusion
- Petites molécules



Hémofiltration

- Convection
- Moyennes molécules



Modalités

- **Intermittente → IRRT**
 - *IHD*: Intermittent hemodialysis
- **Continue → CRRT**
 - *CVVH*: Hemofiltration
 - *CVVHD*: Hemodialysis
 - *CVVHDF*: Hemodiafiltration
 - *SCUF*: Slow continuous ultrafiltration
- **SLED → Hybride**
 - Sustained low efficiency dialysis

IRA aux soins intensifs

IMPORTANCE DU PROBLÈME

Acute Renal Failure in Critically Ill Patients

A Multinational, Multicenter Study

Shigehiko Uchino, MD

JAMA, August 17, 2005—Vol 294, No. 7

- Etude observationnelle épidémiologique: 29'269 patients admis aux soins intensifs
- Prévalence IRA = 5.7%
 - 72% dialysés
 - Mortalité hospitalière = 60%

SAPS II

Table 3. Period Prevalence of Acute Renal Failure and Mortality by Country*

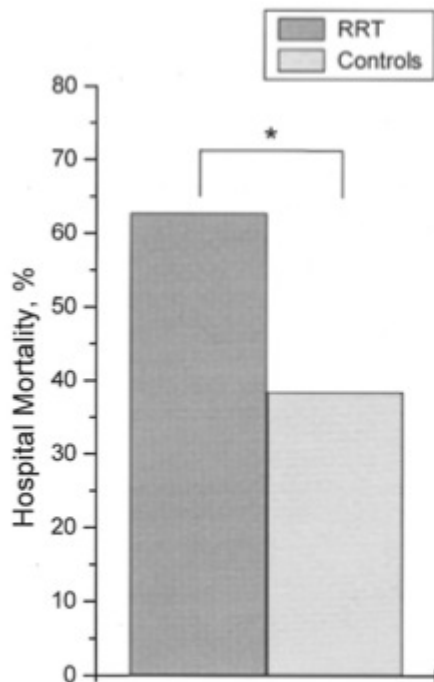
	No. of Participating Centers (N = 54)	No. of Patients (N = 1738)	Period Prevalence (95% CI), %	Predicted Mortality, %†	Hospital Mortality (95% CI), %
Australia	6	293	6.3 (5.6-7.0)	47.0	53.4 (47.7-59.1)
Belgium	3	163	8.8 (7.5-10.1)	43.2	57.7 (50.1-65.3)
Brazil	4	153	4.8 (4.0-5.5)	43.6	76.8 (70.1-83.6)
Canada	2	93	4.6 (3.7-5.6)	56.8	59.8 (49.8-69.8)
China	2	77	8.8 (6.9-10.7)	48.5	61.0 (50.1-71.9)
Czech Republic	1	21	16.8 (10.2-23.4)	44.6	61.9 (41.1-82.7)
Germany	2	129	3.3 (2.7-3.8)	39.4	61.9 (53.4-70.4)
Greece	1	5	2.4 (0.3-4.5)	62.2	80.0 (44.9-100.0)
Indonesia	1	25	4.4 (2.7-6.1)	41.4	72.0 (54.4-89.6)
Israel	1	10	2.1 (0.8-3.4)	61.3	100.0
Italy	6	109	5.4 (4.4-6.4)	32.0	50.5 (41.1-59.8)
Japan	4	90	5.5 (4.4-6.6)	40.8	64.0 (54.1-74.0)
The Netherlands	2	113	6.1 (5.0-7.2)	49.5	62.5 (53.5-71.5)
Norway	2	50	3.7 (2.7-4.7)	46.6	62.0 (48.5-75.5)
Portugal	2	36	22.1 (15.7-28.5)	53.7	63.9 (48.2-79.6)
Russia	1	14	2.6 (1.3-3.9)	82.6	61.5 (35.1-88.0)
Singapore	2	31	6.3 (4.2-8.4)	59.3	74.2 (58.8-89.6)
Spain	2	16	10.5 (5.6-15.3)	32.2	43.8 (19.4-68.1)
Sweden	1	9	4.7 (1.7-7.7)	25.7	22.2 (0-49.4)
Switzerland	1	26	3.2 (2.0-4.4)	44.3	65.4 (47.1-83.7)
United Kingdom	1	52	20.6 (15.6-25.5)	63.7	73.1 (61.0-85.1)
United States	6	194	8.0 (6.8-9.3)	44.2	52.1 (45.0-59.2)
Uruguay	1	29	12.9 (8.5-17.3)	35.6	65.5 (48.2-82.8)
Overall			5.7 (5.5-6.0)	45.6	60.3 (58.0-62.6)

Effect of acute renal failure requiring renal replacement therapy on outcome in critically ill patients*

Philipp G. H. Metnitz, MD, PhD,

Crit Care Med 2002 Vol. 30, No. 9

Cohorte prospective de 17'000 patients admis aux soins intensifs



Contrôles non-RRT matchés pour l'âge et la sévérité de la maladie → Effet « indépendant »

Acute renal failure in patients undergoing renal replacement therapy presents an excess risk of in-hospital death.

Dialyse intermittente VS continue

CONTROVERSE

Acute Renal Failure in Critically Ill Patients

A Multinational, Multicenter Study

Shigehiko Uchino, MD

JAMA, August 17, 2005—Vol 294, No. 7

La CRRT est en général
considérée comme la méthode
de choix aux soins intensifs

Table 1. Characteristics of Patients With Acute Renal Failure and Participating Centers

	No./Total (%)
Men	1105/1738 (63.6)
Renal function	
Normal	966/1738 (55.6)
Chronic impairment	512/1738 (29.5)
Unknown	260/1738 (15.0)
Mechanical ventilation	1312/1722 (76.2)
Vasopressors/inotropes	1189/1721 (69.1)
Mode of RRT	
Continuous	1006/1258 (80.0)
Intermittent	212/1258 (16.9)
Peritoneal dialysis and slow continuous ultrafiltration	40/1258 (3.2)

Littérature: RCT

- **Articles**

- Mehta et al. 2001
- Uehlinger et al. 2005
- Vinsonneau et al. 2006
- ...

- **Problèmes**

- Résultats contradictoires
- Qualité sub-optimale

RCT: Résultats contradictoires

Himmelfarb J: Continuous dialysis is not superior to intermittent dialysis in acute kidney injury of the critically ill patient. *Nat Clin Pract Nephrol* 2007; 3:120–121

Ronco C: Continuous dialysis is superior to intermittent dialysis in acute kidney injury of the critically ill patient. *Nat Clin Pract Nephrol* 2007; 3:118–119

RCT: Résultats contradictoires

Comparison of continuous and intermittent renal replacement therapy for acute renal failure

Dominik E. Uehlinger¹,

Nephrol Dial Transplant (2005) 20: 1630–1637

Table 2. Continuous (CVVHDF) vs intermittent (IHD) renal replacement therapy for acute renal failure: prediction of in-hospital mortality

Variable	Parameter	n	% mortality	OR	P-value
RRT group	CVVHDF	70	47.1	1.00	–
	IHD	55	50.9	1.16	0.36

A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure

RAVINDRA L. MEHTA,

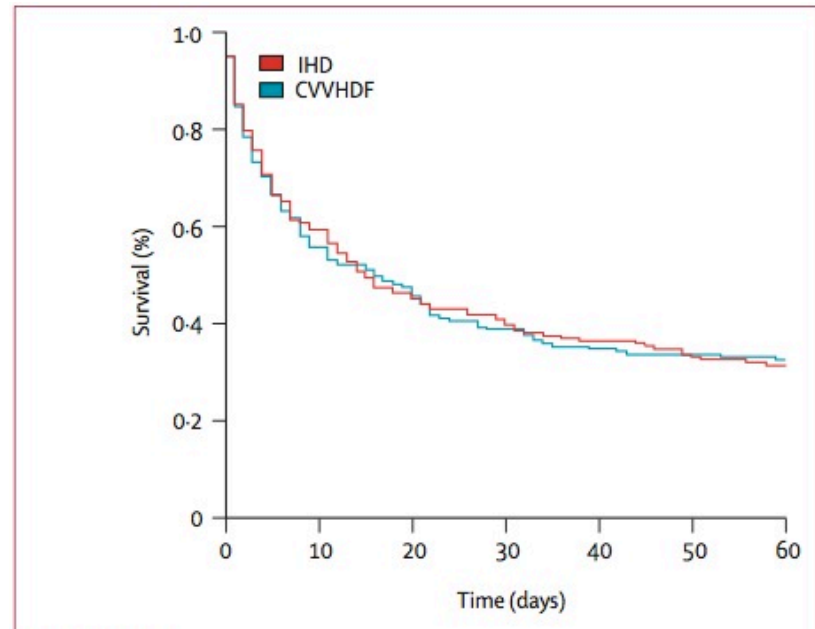
Kidney International, Vol. 60 (2001), pp. 1154–1163

Table 2. CRRT versus IHD for ARF: Prediction of ICU mortality

Variable	Parameter	N	% ICU mortality	OR	CI	P
Gender	Female	40	40	1.00	—	—
	Male	126	54	1.63	0.65–4.13	NS
Liver failure	No	106	35.9	1.00	—	—
	Yes	60	76.7	2.34	1.003–5.46	0.049
APACHE III	≤79	65	26.2	1.00	—	—
	80–100	44	47.7	1.82	0.75–4.43	NS
	>100	57	80.7	3.46	1.23–9.70	0.019
OSF	1–2	59	25.4	1.00	—	—
	3	51	47.1	1.95	0.80–4.74	NS
	>4	56	80.4	3.40	1.15–10.09	0.027
Group	IHD	82	41.5	1.00	—	—
	CRRT	84	59.5	1.58	0.74–3.35	NS

RCT: Vinsonneau et al.

- RCT multicentrique: 359 patients
- IHD vs CVVHDF
- Même filtre, même bain
- Optimisation hémodynamique de l'IHD



RCT: Qualité sub-optimale

- **Puissance**
 - Non calculée ou insuffisante
- **Randomisation**
 - Différence dans les caractéristiques de base
 - Exclusion des patients instables
- **Déroulement**
 - Taux de crossover >10% en intention-to-treat
- **Intervention**
 - Critères d'initiation de RRT non standardisés
 - Dose de dialyse prescrite/administrée non documentée

RCT: Qualité sub-optimale

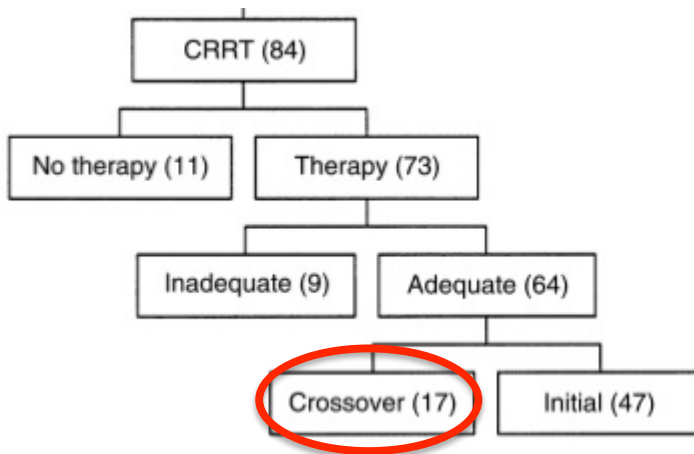
A randomized clinical trial of continuous versus intermittent dialysis for acute renal failure

RAVINDRA L. MEHTA,

Kidney International, Vol. 60 (2001), pp. 1154–1163

Table 1. Characteristics of patients at randomization

	IHD	CRRT	P value
N patients	82	84	
Demographics			
Mean age years	56.3	54.5	NS
% Male	68.3	83.3	<.023
% White	53.7	58.3	NS
% Surgical	31.7	23.8	NS
% ARF on CRF	31.7	23.8	NS
% Oliguric	24.4	20.2	NS
% Ventilated	56.7	64.1	NS
% DNR before consult	1.2	7.1	NS
% ARF 1st ICU day	42.7	45.2	NS
Etiology of ARF			
% Ischemic	53.7	53.6	NS
% Nephrotoxic	14.6	17.9	NS
% Multisystem/GN	7.3	7.1	NS
% Unknown	24.4	21.4	NS
Severity of illness scores			
% Liver failure	29.3	42.9	<.05
APACHE II	23.7	25.5	NS
APACHE III	87.7	96.4	<.045
N organs systems failing	3	3.2	NS



Littérature: Méta-analyses

- **Articles**

- Bagshaw et al. 2008
- Pannu et al. 2008
- Schneider et al. 2013

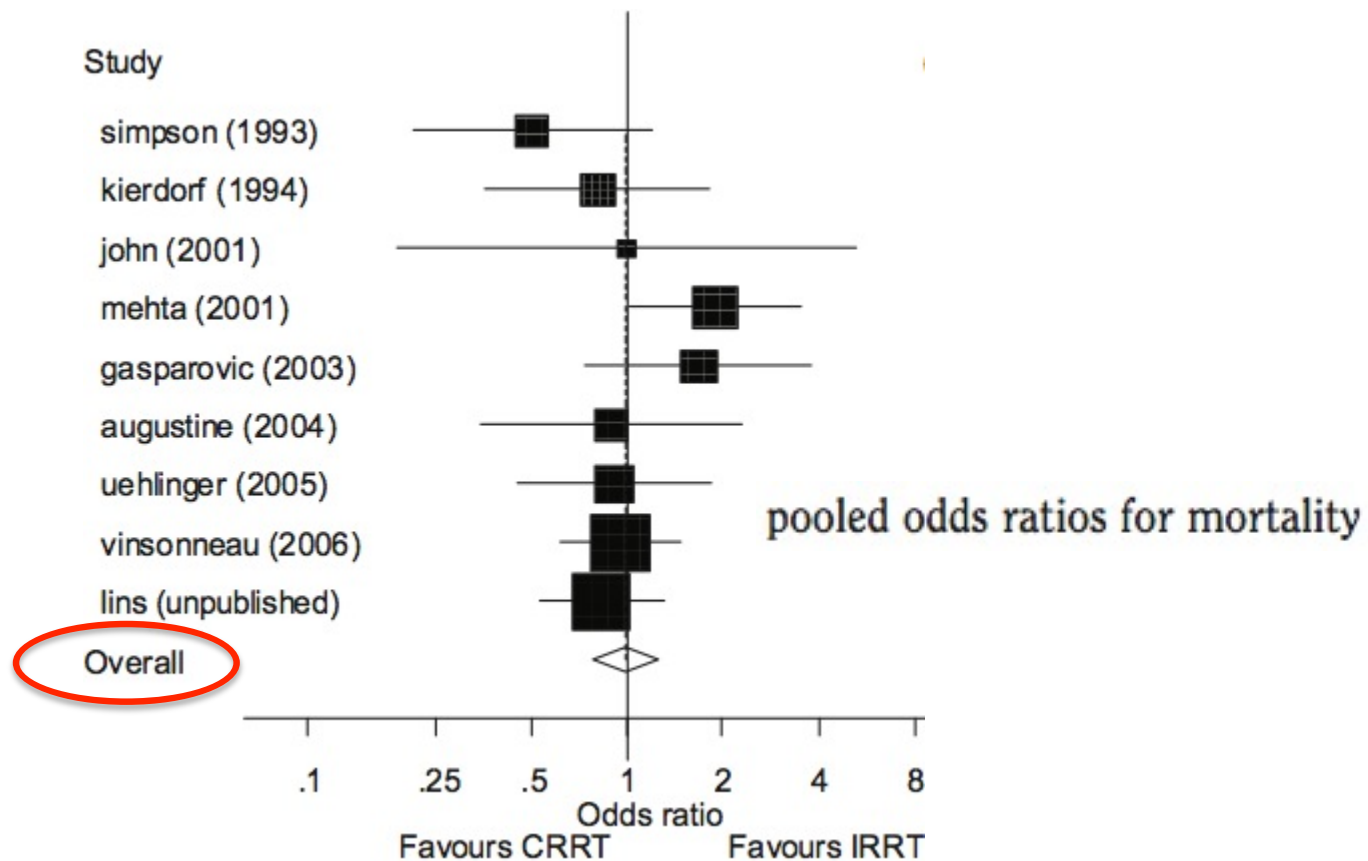
- **Conclusions**

- CRRT et IRRT sont équivalentes
- Qualité insuffisante des études incluse

Continuous versus intermittent renal replacement therapy for critically ill patients with acute kidney injury: A meta-analysis*

Sean M. Bagshaw, MD, MSc; Luc R. Berthiaume, MD; Anthony Delaney, MBBS, MSc; Rinaldo Bellomo, MD

Crit Care Med 2008 Vol. 36, No. 2



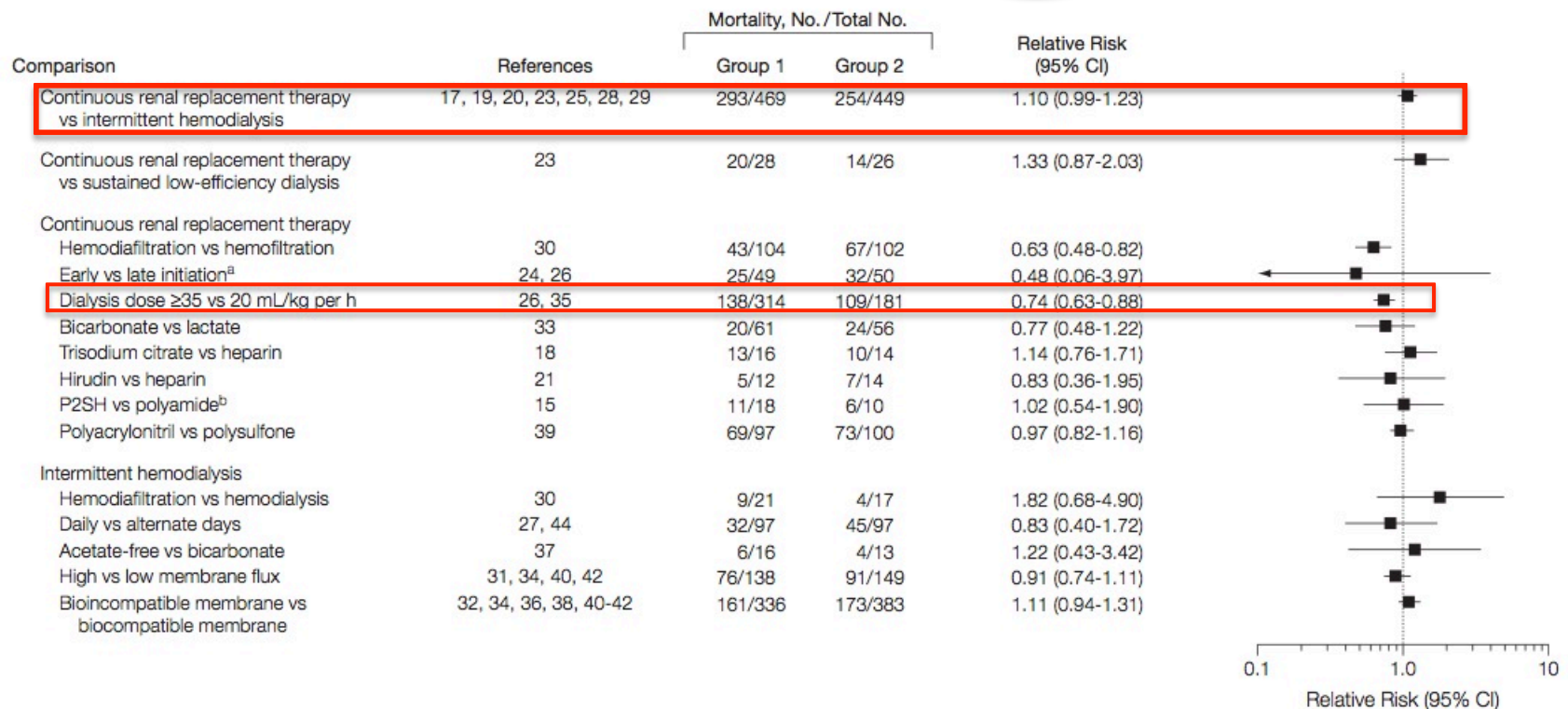
Renal Replacement Therapy in Patients With Acute Renal Failure

A Systematic Review

JAMA, February 20, 2008—Vol 299, No. 7

Neesh Pannu, MD, SM
 Scott Klarenbach, MD, MSc
 Natasha Wiebe, MMath, PStat
 Braden Manns, MD, MSc
 Marcello Tonelli, MD, SM
 for the Alberta Kidney Disease Network

Figure 2. Pooled Effects From Randomized Controlled Trials of Various Interventions on Mortality



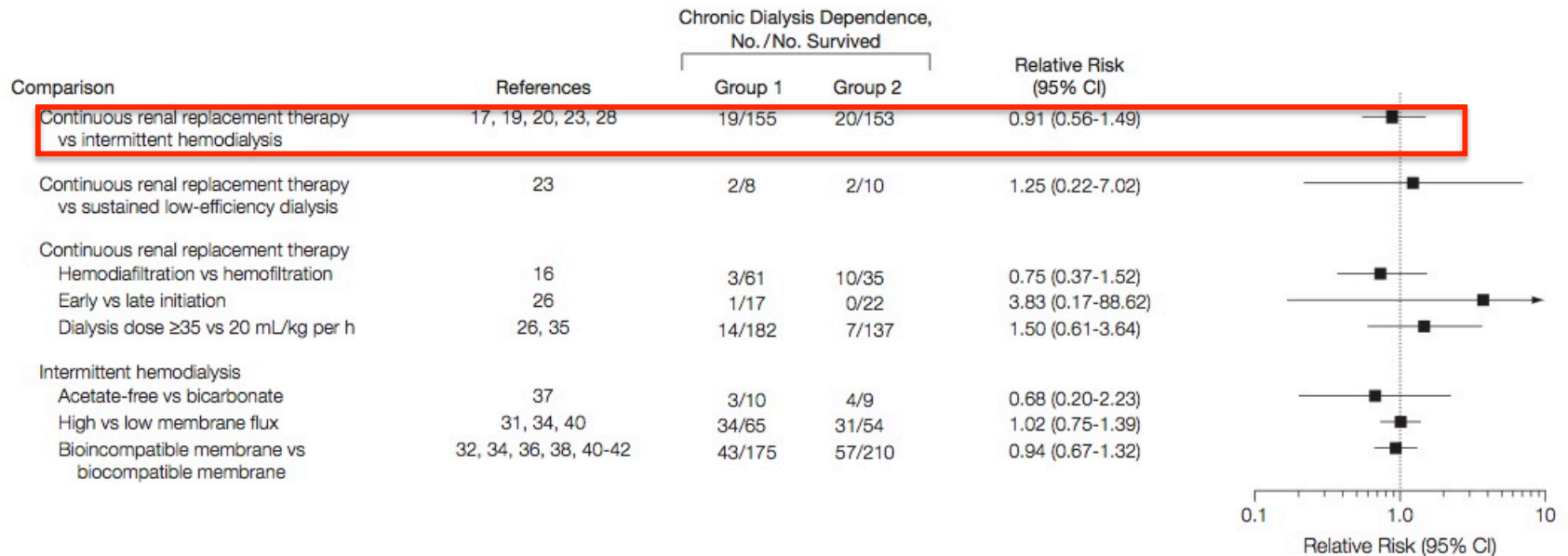
Renal Replacement Therapy in Patients With Acute Renal Failure

A Systematic Review

JAMA, February 20, 2008—Vol 299, No. 7

Neesh Pannu, MD, SM
 Scott Klarenbach, MD, MSc
 Natasha Wiebe, MMath, PStat
 Braden Manns, MD, MSc
 Marcello Tonelli, MD, SM
 for the Alberta Kidney Disease Network

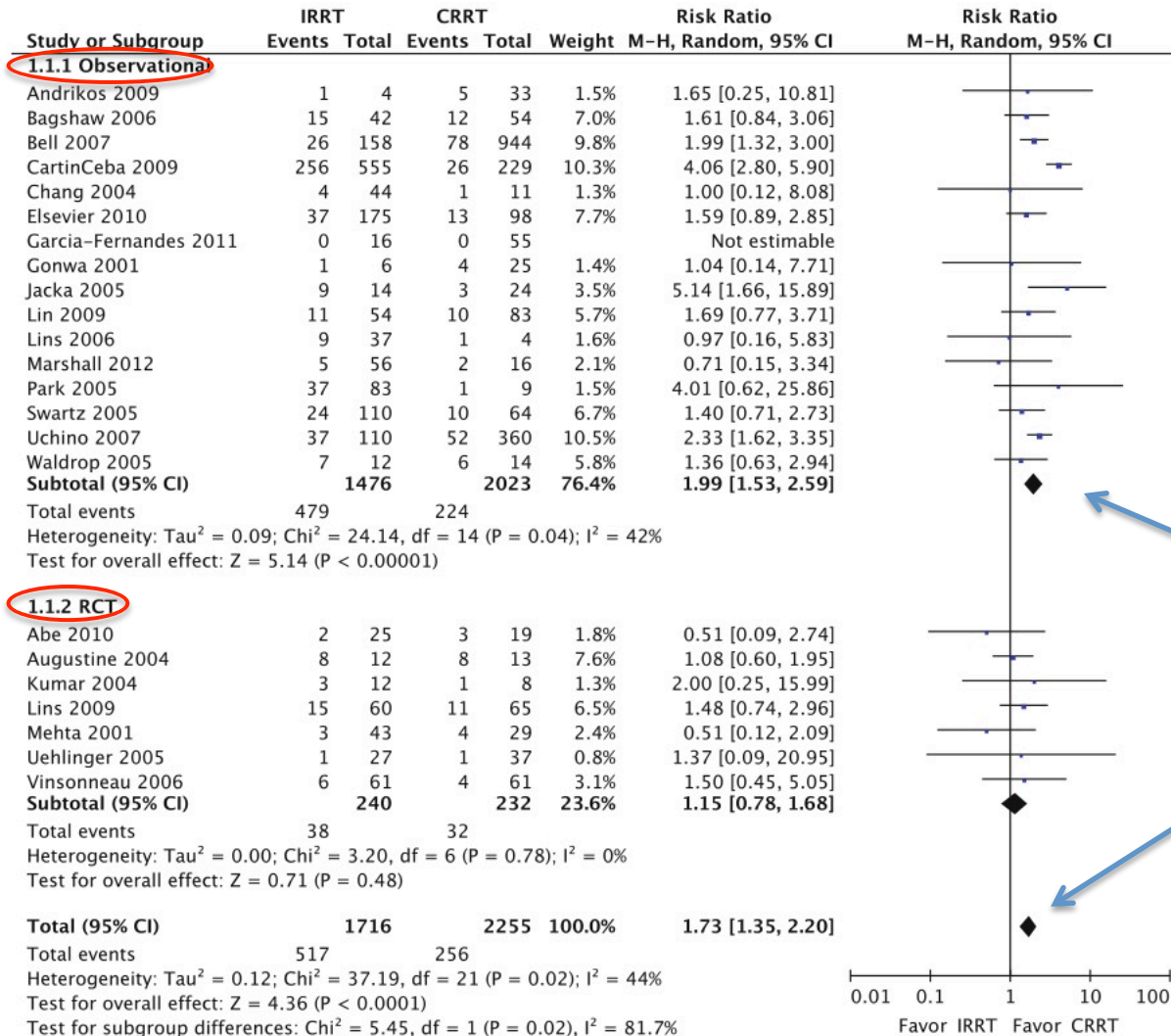
Figure 3. Pooled Effects From Randomized Controlled Trials of Various Interventions on Chronic Dialysis Dependence in Survivors



Choice of renal replacement therapy modality and dialysis dependence after acute kidney injury: a systematic review and meta-analysis

Antoine G. Schneider
 Rinaldo Bellomo
 Sean M. Bagshaw
 Neil J. Glassford
 Serigne Lo
 Min Jun
 Alan Cass
 Martin Gallagher

Intensive Care Med (2013) 39:987–997



Moins de dépendance à la dialyse

Forest plot for dialysis dependence among survivors. Stratified by study design. M-H Mantel-Haenszel

Conclusion

mortality or recovery to RRT independence. There is urgent need for additional high-quality and suitably powered trials to adequately address this issue. (Crit Care Med 2008; 36:610–617)

per hour should be provided. Given the paucity of good-quality evidence in this important area, additional large randomized trials are needed to evaluate clinically important outcomes.

JAMA. 2008;299(7):793-805

www.jama.com

RESEARCH

Open Access

The effect of continuous versus intermittent renal replacement therapy on the outcome of critically ill patients with acute renal failure (CONVINT): a prospective randomized controlled trial

Joerg C Schefold^{1*}, Stephan von Haehling², Rene Pschowski^{1,3}, Thorsten Onno Bender¹, Cathrin Berkmann¹, Sophie Briegel¹, Dietrich Hasper¹ and Achim Jörres¹

Janvier 2014

ETUDE « CONVINT »

Méthodes: Design

- RCT unicentrique open-label de 2002 à 2007
- Hôpital universitaire, soins intensifs de médecine
- **Inclusion**
 - Tout adulte admis aux SI avec IRA nécessitant une RRT
 - Urémie symptomatique, oligo-anurie, hypervolémie réfractaire, urée >36 mmol/l, GFR <0.1 ml/kg/min, pH <7.2 réfractaire, hyperK+ réfractaire
- **Exclusion**
 - IRC pré-existante (créat >264 umol/l)
 - Dialysés
 - Tranplantés

Méthodes: Protocole

- **Groupe 1: IHD**

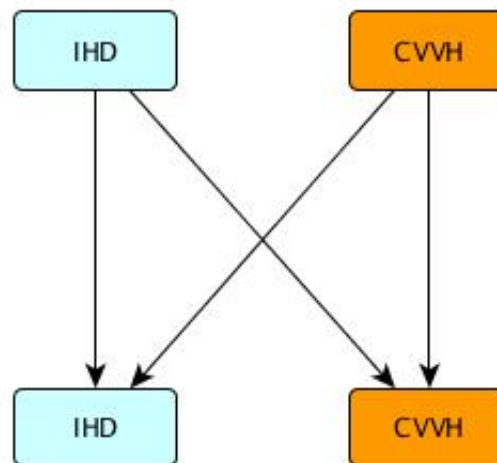
- HD seule 4 heures par jour
- Débit sang 200 – 250 ml/min
- Débit dialysat 500 ml/min
- Filtre??

- **Groupe 2: CVVH**

- Hémofiltration seule en post-dilution
- Débit sang 200 ml/min
- Dose 35 ml/kg/h
- Filtre??

Méthodes: Protocole

- Crossover autorisé (par le médecin en charge)
- **IHD → CVVH**
 - Instabilité HD
- **CVVH → IHD**
 - Electrolytes, acide-base
 - Dose de dialyse
 - Anticoagulation
 - Mobilisation



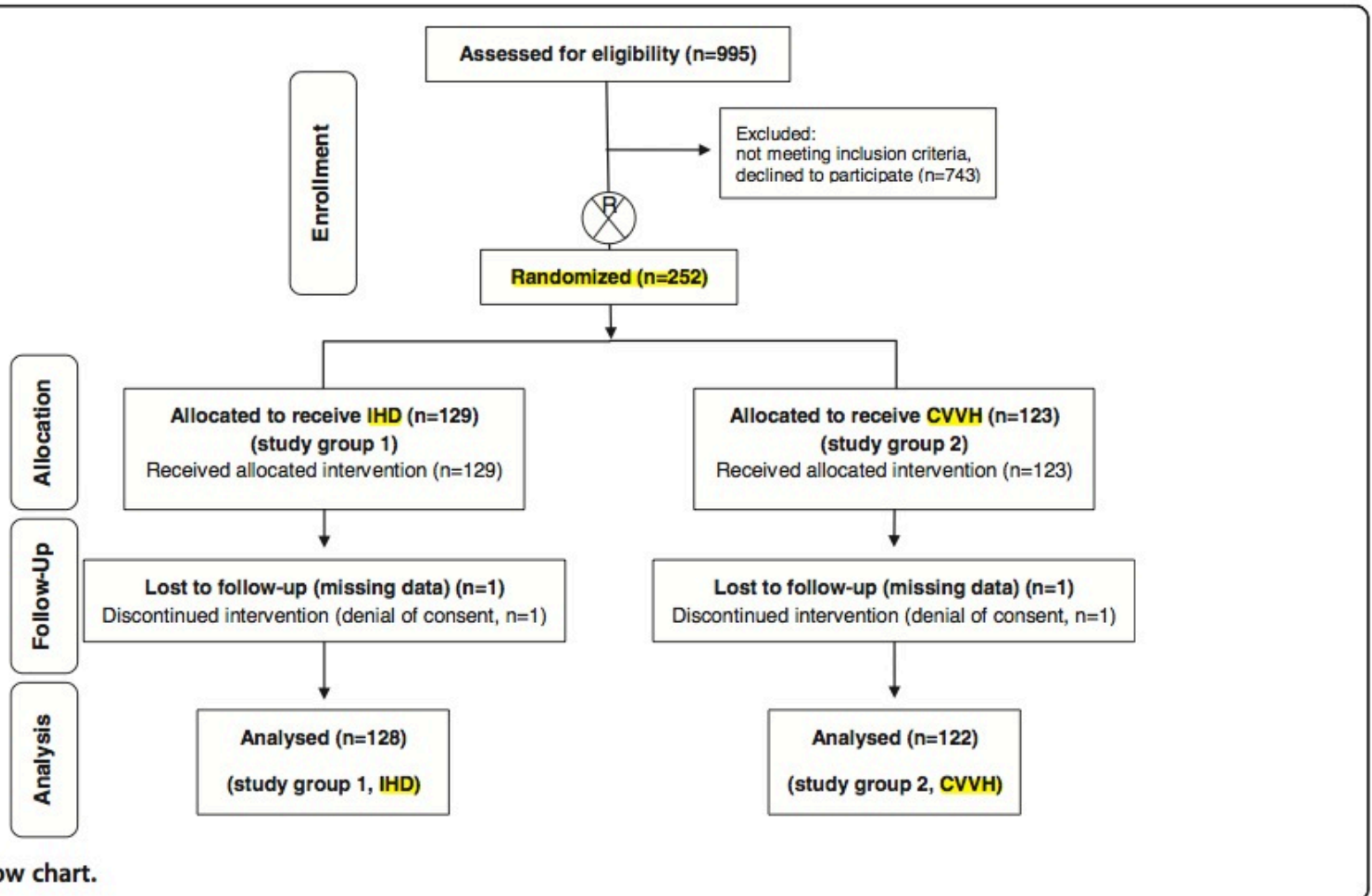
Méthodes: Outcome

- **Outcome primaire**
 - Survie à 14 jours après la fin de la RRT
- **Outcome secondaire**
 - Mortalité de toute cause à 14 et 30 jours
 - Nb de jours aux SI/hôpital
 - Nb de jours avec/sans RRT
 - Etc.

Méthodes: Analyses statistiques

- **Puissance** estimée: 200 patients par groupe
 - ➔ Interruption prématurée après inclusion de 252 patients
- Analyse en **ITT**
 - ➔ En fonction du groupe initial
- Analyse de **sous-groupe**
 - ➔ Patients dépendants des amines
 - ➔ Patients crossover

Résultats: Flowchart



Résultats: Baseline

Serum creatinine (mg/dl)		3.64 ± 2.3	3.57 ± 1.9	0.81
Serum urea (mg/dl)		159.7 ± 86.5	156.7 ± 77.1	0.77
Serum potassium (mM)		4.66 ± 0.8	4.65 ± 0.9	0.91
Baseline blood pH		7.32 ± 0.2	7.32 ± 0.1	0.82
Baseline HCO ₃ ⁻		22.6 ± 6.8	21.8 ± 5.4	0.34
Urine output (within 24 hours before randomization; ml)		927.1 ± 1318.4	708.5 ± 937.8	0.10
Days in ICU until randomization		1.0 [0–3.0] ^b	1.0 [0–2.3] ^b	0.82
Days from ICU admission until start of RRT		1.0 [0–4.0] ^b	1.0 [0–3.0] ^b	0.55
Need for mechanical ventilation (at study day 1)		113 (88.3%)	103 (84.4%)	0.88
paO ₂ /FiO ₂ ratio (in all patients at study day 1)		197.3 ± 107.9	208.7 ± 106.8	0.45
Need for (any) vasopressor (at study day 1)		104 (81.2%)	106 (86.9%)	0.79 ^{a*}
Key hemodynamic variables (at study day 1)	Heart rate (/min)	104.0 ± 26.1	104.7 ± 20.9	0.81
	Systolic blood pressure (mm Hg)	111.6 ± 22.5	109.8 ± 19.4	0.51
	Diastolic blood pressure (mm Hg)	56.4 ± 11.1	53.0 ± 13.6	0.04
	Central venous pressure (cmH ₂ O)	14.7 ± 5.3	14.2 ± 5.41	0.52
	Cardiogenic failure/ shock	26 (20.3%)	20 (16.4%)	0.61 ^{a*}
	Sepsis-induced	85 (66.4%)	85 (69.7%)	0.89*
	Hemorrhagic	2 (1.6%)	3 (2.5%)	0.96*
	No shock present	7 (5.5%)	5 (4.1%)	0.85*
	Obstruction-induced	0	3 (2.5%)	0.24*
	Unknown	8 (6.3%)	9 (7.4%)	0.94*
Reason for ARF/need for RRT (number of patients)				
APACHE-II score		28.5 ± 7.9	28.8 ± 9.6	0.79
SAPS-II score		66.1 ± 18.1	63.8 ± 17.6	0.34
SOFA score		13.2 ± 3.9	13.0 ± 4.0	0.66

Résultats: Follow-Up

- Pas de différence des paramètres de suivi (clinique et biologique) entre les 2 groupes
- **Dose de dialyse (CVVH)**
 - 31 ml/kg/h (càd 88% de la dose prescrite)
- **Anticoagulation (IHD et CVVH)**
 - HNF >98%

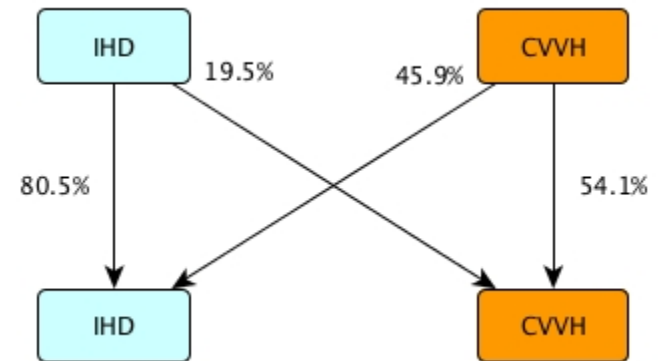
Résultats: Crossover

- **IHD → CVVH**

- Instabilité HD
- Surcharge volémique

- **CVVH → IHD**

- Coagulation/Anticoagulation
- Electrolytes, acide-base
- Mobilisation



Résultats: Outcomes

Mortalité



Analyse ITT



		iHD group (n = 128)	CVVH group (n = 122)	P value
Survival at 14 days after RRT		39.5%	43.9%	0.81 ^a
14-day mortality rate		43.6%	37.8%	0.63 ^a
30-day mortality rate		52.4%	45.4%	0.60 ^a
All-cause intrahospital mortality rate (last contact)		60.3%	54.6%	0.72 ^a
Days until death		15.6 ± 44.5	18.5 ± 48.9	0.71
Days until death on ICU		15.5 ± 45.9	18.4 ± 50.0	0.73
Days until hospital discharge (in survivors)		51.2 ± 47.1	48.7 ± 49.7	0.78
Days in ICU		25.2 ± 40.1	22.3 ± 26.1	0.50
Days in hospital		33.9 ± 49.3	32.4 ± 37.4	0.79
Suspected reason for death (multiple possible)	Cardiac failure	31	22	0.42 ^a
	Pulmonary failure	39	31	0.59 ^a
	Sepsis	56	45	0.55 ^a
	CNS	7	6	0.92 ^a
	Hemorrhagy	5	4	0.93 ^a
	Withdrawal of therapy	4	2	0.74 ^a
	Days on RRT		17.2 ± 37.1	13.7 ± 17.9
Dialysis-free days		4.2 ± 9.6	3.1 ± 9.0	0.38
RRT switch (number of patients)		25 (19.5%)	56 (45.9%)	0.002 ^a
Number of patients on RRT (% of survivors, days after ICU admission)	At 21 days	20 (32.3%)	20 (29.9%)	0.97 ^a
	At 60 days	14 (26.4%)	13 (22.8%)	0.90 ^a
Serum creatinine at hospital discharge/last contact (in survivors; mg/dl)		2.18 ± 1.8	2.12 ± 1.7	0.85
Total days on vasopressors		4.3 ± 3.7	4.5 ± 3.7	0.75
Cumulative vasopressor dose (g)	Epinephrine	0.70	0.64	0.96
	Norepinephrine	19.1	18.5	0.30
	Dobutamine	150.2	137.9	0.56
Total days on mechanical ventilation		8.1 ± 8.8	7.2 ± 6.5	0.34
Total fluid balance (L)		20.5 ± 23.2	24.9 ± 28.4	0.19

Pronostic rénal



Résultat: Outcomes

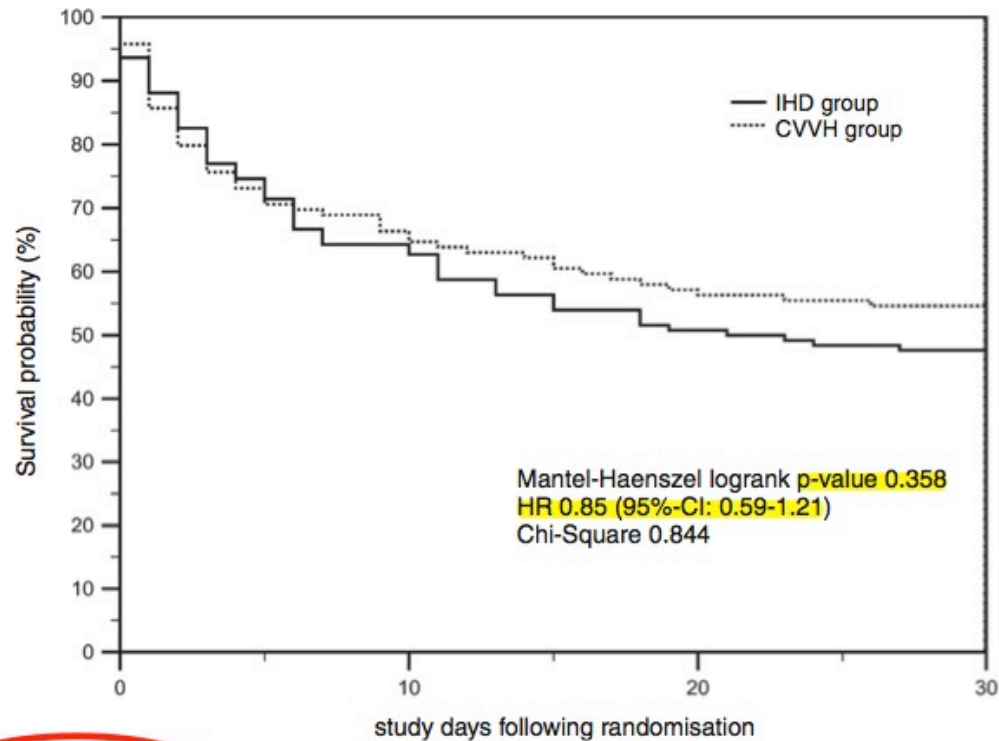
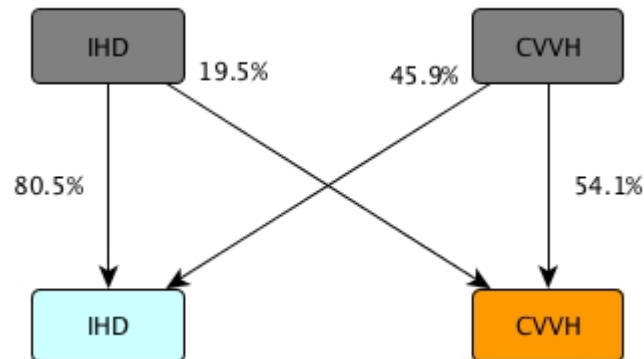


Figure 2 Kaplan-Meier survival estimates for patients randomized to IHD (full line, $n = 128$) and CVVH (dotted line, $n = 122$) are illustrated (total study population). Mantel-Haenszel log-rank P value, hazard ratio (HR) including 95% CI and χ^2 is given.

Résultats: Sous-groupes

- **Crossover**

- Pas de modification des outcomes principaux



- **Amines**

- Pas de modification des outcomes principaux

Résultats: Sous-groupes

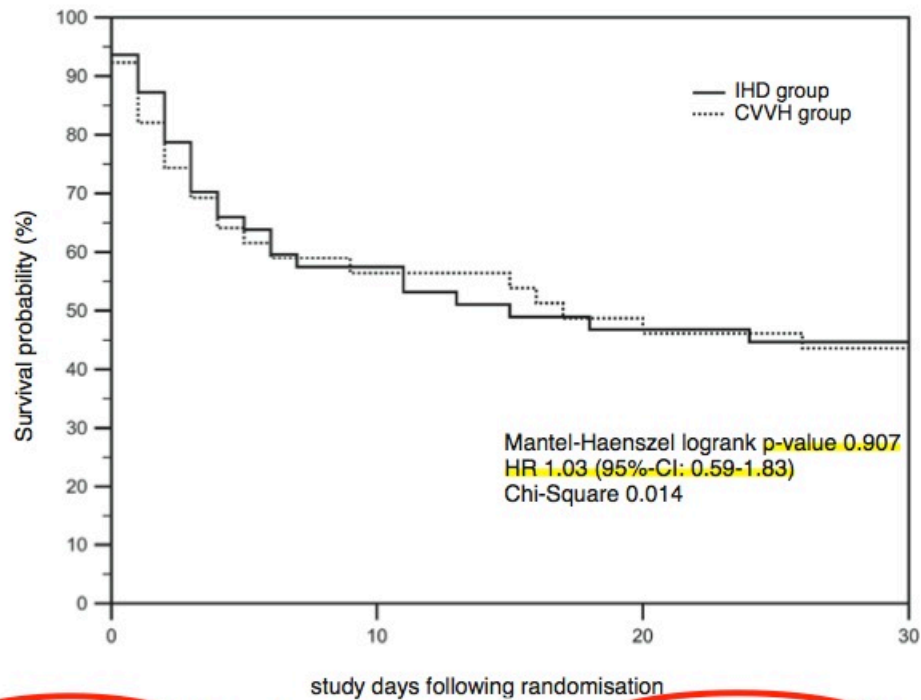


Figure 3 Kaplan-Meier survival estimates for the subpopulation of patients with high vasopressor need (overall sample; high vasopressor use defined as $> 0.3 \mu\text{g/kg/min}$ at any point in time during the study interval) in the IHD (full line, $n = 47$) versus CVWH (dotted line, $n = 40$) groups are illustrated. Mantel-Haenszel log-rank P value, hazard ratio (HR), including 95% CI and χ^2 is given.

Discussion

- **Population**

- IRC (créatinine > 264 $\mu\text{mol/l}$) exclus
- Atteinte sévère

→ *Reproductibilité?*

Need for (any) vasopressor (at study day 1)	104 (81.2%)	106 (86.9%)
Need for mechanical ventilation (at study day 1)	113 (88.3%)	103 (84.4%)
30-day mortality rate	52.4%	45.4%

- **Modalités**

- IRR: IHD 4h 1x/j
- CRRT: CVVH 35 ml/kg/h

→ *Reproductibilité?*

Discussion

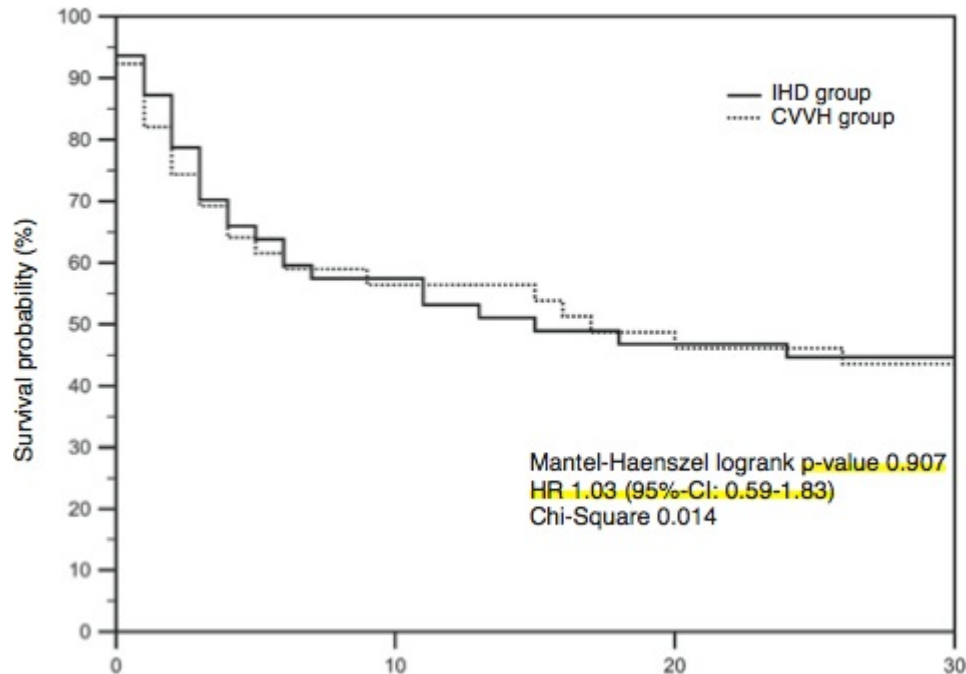
- **Dose de dialyse**
 - Prescrite: 35 ml/kg/h
 - Délivrée: 31 ml/kg/h

In conclusion, there are now consistent data from two large multicenter trials showing no benefits of increasing CRRT doses in AKI patients above effluent flows of 20–25 ml/kg/h. In clinical practice, in order to achieve a delivered dose of 20–25 ml/kg/h, it is generally necessary to prescribe in the range of 25–30 ml/kg/h, and to minimize interruptions in CRRT.



Discussion

- **Instabilité HD**



CAVE: Analyse de sous-groupe!

In conclusion, in the presence of hemodynamic instability in patients with AKI, **CRRT** is preferable to standard IHD.

Limitations

- **Puissance insuffisante**
 - Arrêt prématuré (équipement et protocoles)
 - Seulement 63% de la taille d'échantillon prévue
 - Analyse rétrospective hypothétique: Mêmes résultats

- **Crossover**
 - Biais possible en ITT
 - Sous-groupe crossover: Pas de modification des outcomes principaux

Dialyse aux soins intensifs

QUELQUES COMMENTAIRES GÉNÉRAUX

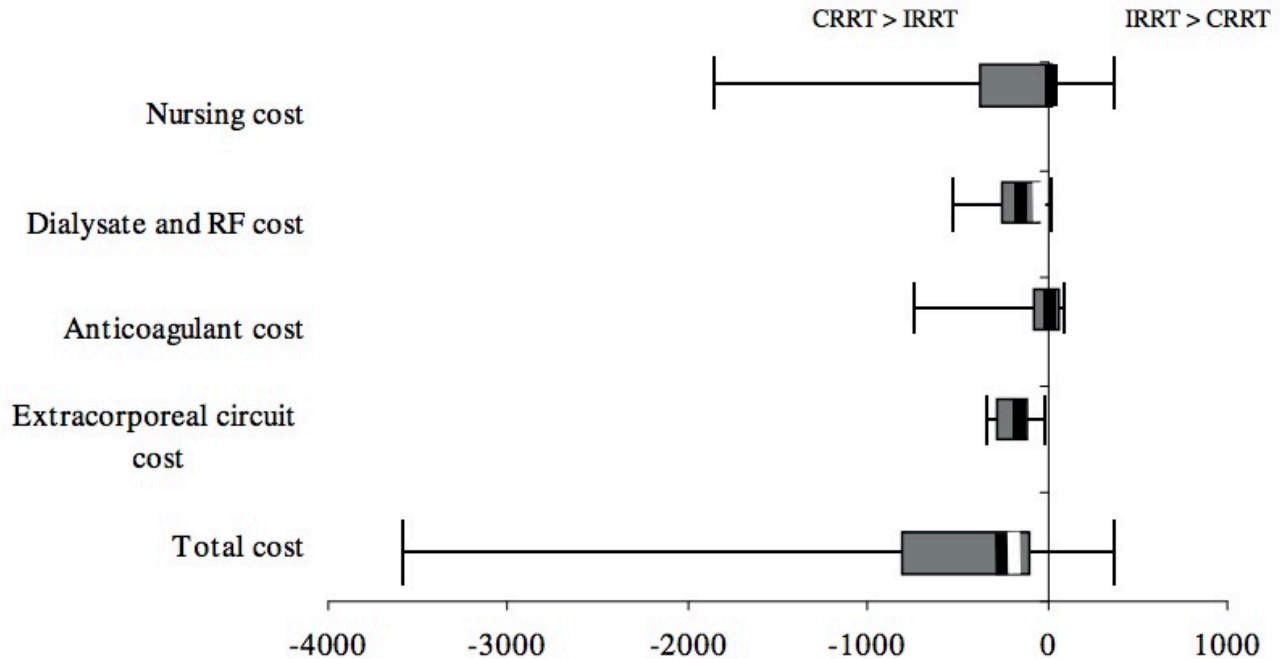
Modalités non standardisées

- CRRT: HD, HF, HDF, SLED, ...?
- IRRT: 2h? 4h? 1x/j, 1x/2j, ...?
- Dose de dialyse?
- Machines, filtres, ...?

Source	Comparison	Intervention					Control				
		Technique (Device)	Membrane Material (Flux)	Buffer	Anti-coagulant	Dosage (Schedule)	Technique (Device)	Membrane Material (Flux)	Buffer	Anti-coagulant	Dosage (Schedule)
Uehlinger, ¹⁹ 2005	CRRT vs IHD	CWHDF (Prisma)	PAN (high)	L	H/none	2 L/h or UCI ≈ 30 mL/min	IHD (MiroClav)	PS (high)	B	H/none	UCI ≈ 200 mL/min (3-4 h/session)
Augustine, ²⁰ 2004	CRRT vs IHD	CWHD (NA)	PS (low)	B	H/none	Kt/V 3.6/wk	IHD (NA)	PS (low)	B	H/none	Kt/V 3.6/wk (3 sessions/wk)

Neesh Pannu, MD, SM

Coûts



- Cost differences are highly variable across centers and include scenarios in which either therapy is more or less expensive compared with the other.

Conclusion

Table 22 | Theoretical advantages and disadvantages of CRRT, IHD, SLED, and PD

Modality	Potential setting in AKI	Advantages	Disadvantages
IHD	Hemodynamically stable	<p>Rapid removal of toxins and low-molecular-weight substances</p> <p>Allows for "down time" for diagnostic and therapeutic procedures</p> <p>Reduced exposure to anticoagulation</p> <p>Lower costs than CRRT</p>	<p>Hypotension with rapid fluid removal</p> <p>Dialysis disequilibrium with risk of cerebral edema</p> <p>Technically more complex and demanding</p>
CRRT	Hemodynamically unstable Patients at risk of increased intracranial pressure	<p>Continuous removal of toxins</p> <p>Hemodynamic stability</p> <p>Easy control of fluid balance</p> <p>No treatment-induced increase of intracranial pressure</p> <p>User-friendly machines</p>	<p>Slower clearance of toxins</p> <p>Need for prolonged anticoagulation</p> <p>Patient immobilization</p> <p>Hypothermia</p> <p>Increased costs</p>

Conclusion

In conclusion, **no RRT is ideal for all patients with AKI.** Clinicians should be aware of the pros and cons of different RRTs, and **tailor RRT** on the basis of the individual and potentially changing needs of their patients. Besides the individual patient's characteristics, the available expertise and resources may also be an important determinant of the ultimate choice.

