



EER: quand et comment ?

AER

Lyon, 23 novembre 2017

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Service de Médecine Intensive - Réanimation

Clermont-Ferrand

Conflits d'intérêts

- Hémotec

Quelle insuffisance rénale en réa ?

Acute Renal Failure in Critically Ill Patients

Shigehiko Uchino, MD

A Multinational, Multicenter Study

JAMA, August 17, 2005—Vol 294, No. 7 813

Table 2. Medical and Surgical Intensive Care Unit Admissions and Contributing Factors to Acute Renal Failure

	No. (%)
Contributing factors (n = 1726)	
Septic shock	820 (47.5)
Major surgery	592 (34.3)
Cardiogenic shock	465 (26.9)
Hypovolemia	442 (25.6)
Drug-induced	328 (19.0)
Hepatorenal syndrome	99 (5.7)
Obstructive uropathy	45 (2.6)
Other	211 (12.2)

**Sepsis: 1^{ère} cause
d'IRA (> 40%)**

54 international ICU : 1 738 IRA (6% des admiss)

Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study

Eric A. J. Hoste Intensive Care Med (2015) 41:1411–1423

97 international ICU : 666 AKI (32% des admiss)

Table 2 Variables at the time of acute kidney injury (n = 666)

Etiology of AKI	
Sepsis	271 (40.7 %)
Hypovolemia	227 (34.1 %)
Drug related	96 (14.4 %)
Cardiogenic shock	88 (13.2 %)
Hepatorenal syndrome	21 (3.2 %)
Obstruction of the urine outflow tract	9 (1.4 %)

Quelle EER en réa ?

Acute Renal Failure in Critically Ill Patients

A Multinational, Multicenter Study

CARING FOR THE
CRITICALLY ILL PATIENT

JAMA, August 17, 2005—Vol 294, No. 7

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)

Epidemiology of acute kidney injury in critically ill patients: the multinational AKI-EPI study

Eric A. J. Hoste Intensive Care Med (2015) 41:1411–1423

97 international ICU : 666 AKI (32% des admiss)

Durant la 1ère semaine d'EER:

- CRRT : 75% (615 séances)
- IHD: 24% (197 séances)
- Dialyses péritonéales: 0,7% (6 séances)

Objectifs de l'EER

```
graph TD; A[Objectifs de l'EER] --> B[Suppléer le rein: homéostasie]; A --> C[Immunomodulation:]; B --- D["- ionique<br/>- acido-basique<br/>- surcharge hydro-sodée"]; C --- E["Éliminer<br/>les médiateurs inflammatoires<br/>du sepsis"]
```

Suppléer le rein: homéostasie

- ionique**
- acido-basique**
- surcharge hydro-sodée**

Immunomodulation:

**Éliminer
les médiateurs inflammatoires
du sepsis**

Quelle EER en réa ?

Impact of continuous venovenous hemofiltration on organ failure during the early phase of severe sepsis: A randomized controlled trial*

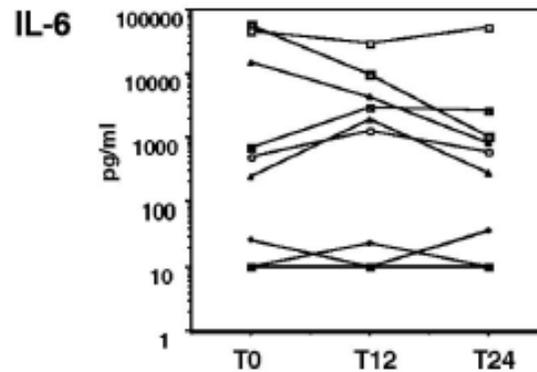
Payen CCM 09

CVVH dans les 24h de la 1ère défaillance d'organe due à un sepsis

CVVH (25ml/kg/h) pdt 96h

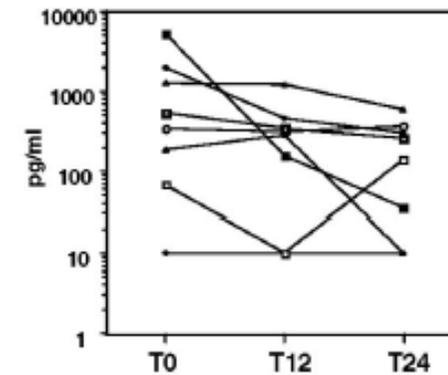
n = 37

Hemofiltrated patients

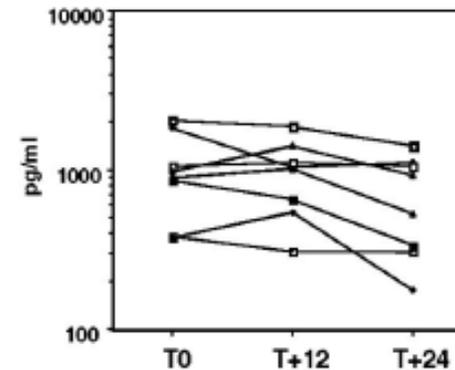
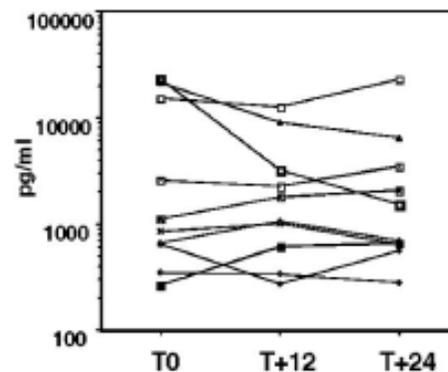


n = 39

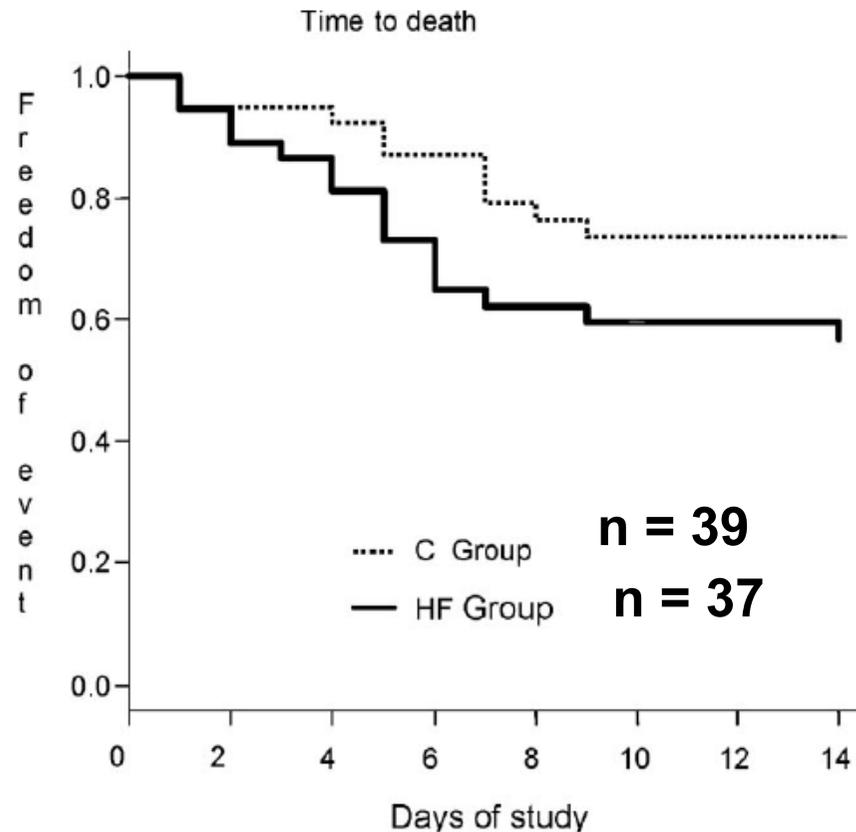
Non-hemofiltrated patients



MCP-1



Quelle EER en réa ?



Payen CCM 09

Conclusion: These data suggest that early application of standard continuous venovenous hemofiltration is deleterious in severe sepsis and septic shock. This study does not rule out an effect of high-volume hemofiltration (>35 mL/kg/hr) on the course of sepsis. (Crit Care Med 2009; 37:803–810)

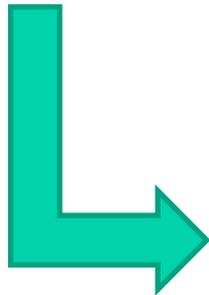
Objectifs de l'EER

Suppléer le rein: homéostasie

- ionique
- acido-basique
- surcharge hydro-sodée

Immunomodulation:

**Éliminer
les médiateurs inflammatoires
du sepsis**



Quand ??

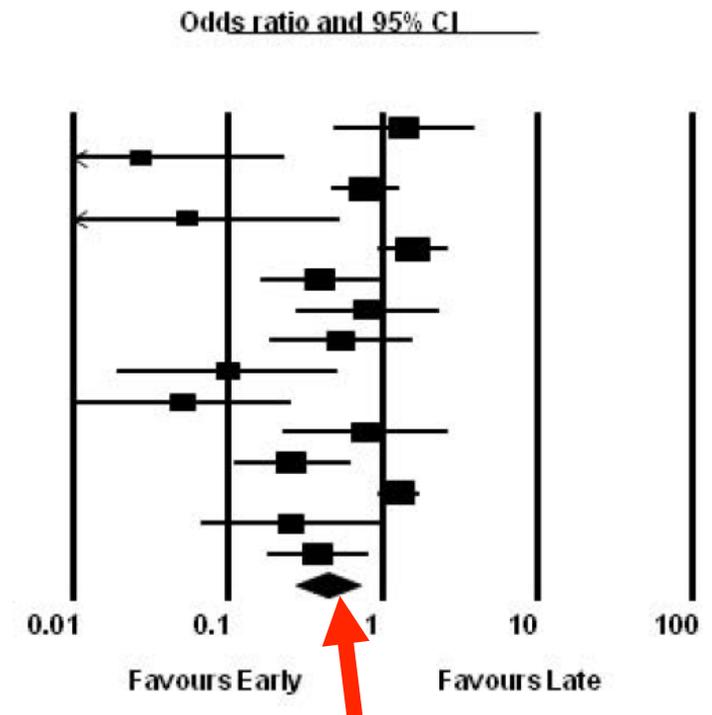
Timing de début

A comparison of early versus late initiation of renal replacement therapy in critically ill patients with acute kidney injury: a systematic review and meta-analysis



Karvellas *et al. Critical Care* 2011,

Study name	Subgroup within study	Statistics for each study				
		Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Bouman 2002	Mixed	1.375	0.487	3.884	0.601	0.548
Sugahara 2004	Surgery	0.028	0.003	0.231	-3.318	0.001
Liu 2006	Mixed	0.773	0.460	1.298	-0.974	0.330
Sabater 2008	Mixed	0.055	0.006	0.524	-2.520	0.012
Bagshaw 2010*	Mixed	1.563	0.933	2.619	1.697	0.090
Gettings 1999	Surgery	0.399	0.164	0.973	-2.019	0.043
Elahi 2004	Surgery	0.800	0.273	2.341	-0.407	0.684
Demirkilic 2004	Surgery	0.533	0.183	1.552	-1.154	0.249
Andrade 2007	Mixed	0.100	0.019	0.515	-2.752	0.006
Manche 2008	Surgery	0.051	0.010	0.256	-3.623	0.000
Iyem 2009	Surgery	0.778	0.229	2.644	-0.403	0.687
Shiao 2009	Surgery	0.260	0.110	0.614	-3.075	0.002
Bagshaw 2009 adj	Mixed	1.250	0.915	1.708	1.401	0.161
Wu 2007 adj	Surgical	0.259	0.068	0.988	-1.977	0.048
Carl 2010 adj	Mixed	0.380	0.177	0.816	-2.482	0.013
		0.446	0.276	0.723	-3.279	0.001



Classification KDIGO



<http://www.kidney-international.org>

contents

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VOL 2 | SUPPLEMENT 1 | MARCH 2012



KDIGO Clinical Practice Guideline for Acute Kidney Injury



2.1.1: AKI is defined as any of the following (*Not Graded*):

- Increase in SCr by ≥ 0.3 mg/dl (≥ 26.5 μ mol/l) within 48 hours; or
- Increase in SCr to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or
- Urine volume < 0.5 ml/kg/h for 6 hours.

2.1.2: AKI is staged for severity according to the following criteria (Table 2). (*Not Graded*)

2.1.3: The cause of AKI should be determined whenever possible. (*Not Graded*)

Table 2 | Staging of AKI

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR ≥ 0.3 mg/dl (≥ 26.5 μ mol/l) increase	< 0.5 ml/kg/h for 6–12 hours
2	2.0–2.9 times baseline	< 0.5 ml/kg/h for ≥ 12 hours
3	3.0 times baseline OR Increase in serum creatinine to ≥ 4.0 mg/dl (≥ 353.6 μ mol/l) OR Initiation of renal replacement therapy OR, In patients < 18 years, decrease in eGFR to < 35 ml/min per 1.73 m ²	< 0.3 ml/kg/h for ≥ 24 hours OR Anuria for ≥ 12 hours

Timing de début

	Early	Late
I.D.E.A.L.-I.C.U. (Initiation of Dialysis EARly Versus Late in Intensive Care Unit)		
<i>This study is currently recruiting participants.</i> <i>Verified June 2013 by Centre Hospitalier Universitaire Dijon</i>		
ClinicalTrials.gov Identifier: NCT01682590		
	< 12h	48-60h
		F-RIFLE
Initiation Strategies for Renal-Replacement Therapy in the Intensive Care Unit		
NEJM, May, 2016		
	< 6h	KDIGO stage 3 Urea >40 mmol/L Oliguria > 3d
Effect of Early vs Delayed Initiation of Renal Replacement Therapy on Mortality in Critically Ill Patients With Acute Kidney Injury		
The ELAIN Randomized Clinical Trial		
	< 8h	KDIGO stage 2 +NGAL>150ng/ml <12h
		KDIGO stage 3

JAMA. 2016;315(20):2190-2199.

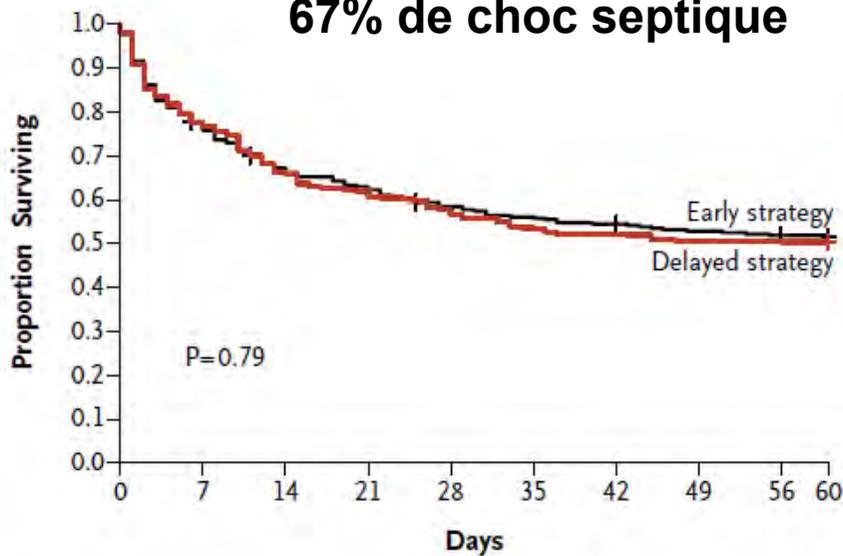
Timing de début

AKIKI study, Gaudry, NEJM, 2016

early
KDIGO stage 3
< 6h

late
Urea >40 mmol/L
Oliguria > 3d

67% de choc septique



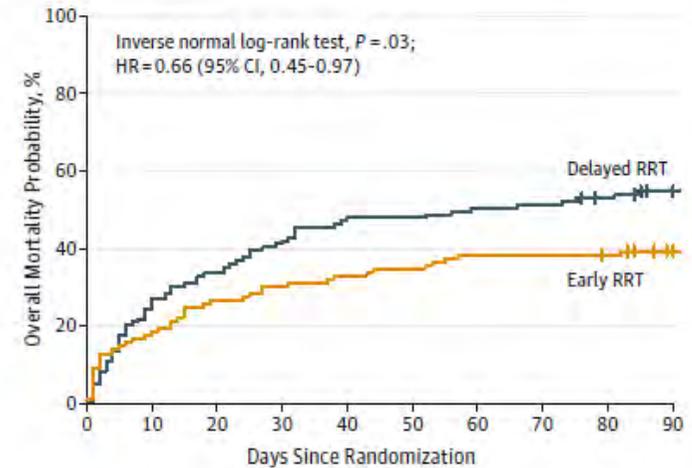
No. at Risk	0	7	14	21	28	35	42	49	56	60
Early strategy	311	241	207	194	179	172	167	161	158	157
Delayed strategy	308	239	204	191	178	165	161	156	156	155

ELAIN study, Zarbock, Jama, 2016

early
KDIGO stage 2
+NGAL>150ng/ml
< 8h

late
KDIGO stage 3
<12h

Figure 2. Mortality Probability Within 90 Days After Study Enrollment for Patients Receiving Early and Delayed Initiation of Renal Replacement Therapy (RRT)



No. at risk	0	10	20	30	40	50	60	70	80	90
Early RRT	112	92	82	78	75	73	69	69	66	55
Delayed RRT	119	90	79	70	63	62	59	58	54	48

Timing de début

Fluid balance and mortality in critically ill patients with acute kidney injury: a multicenter prospective epidemiological study



Wang et al. *Critical Care* (2015) 19:371

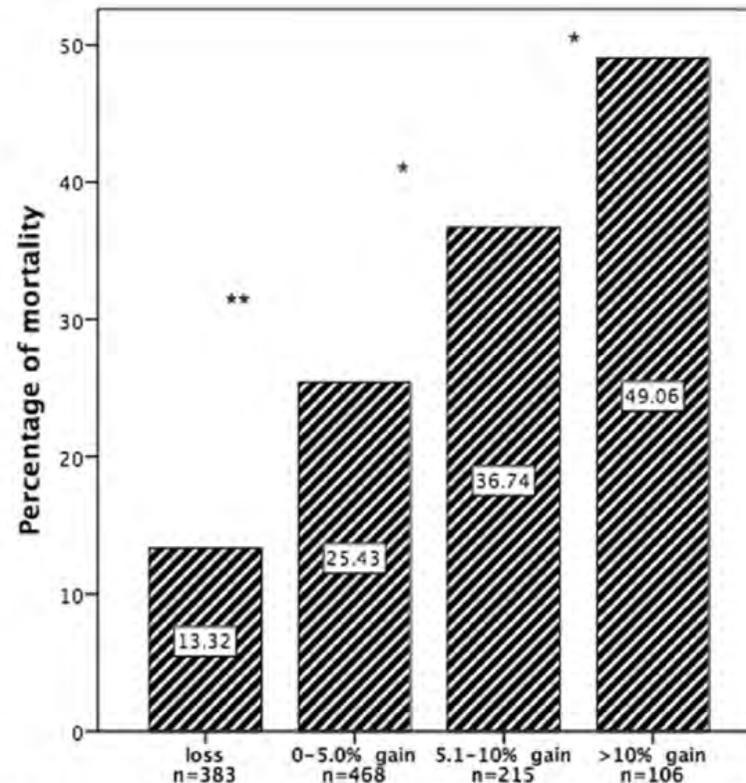


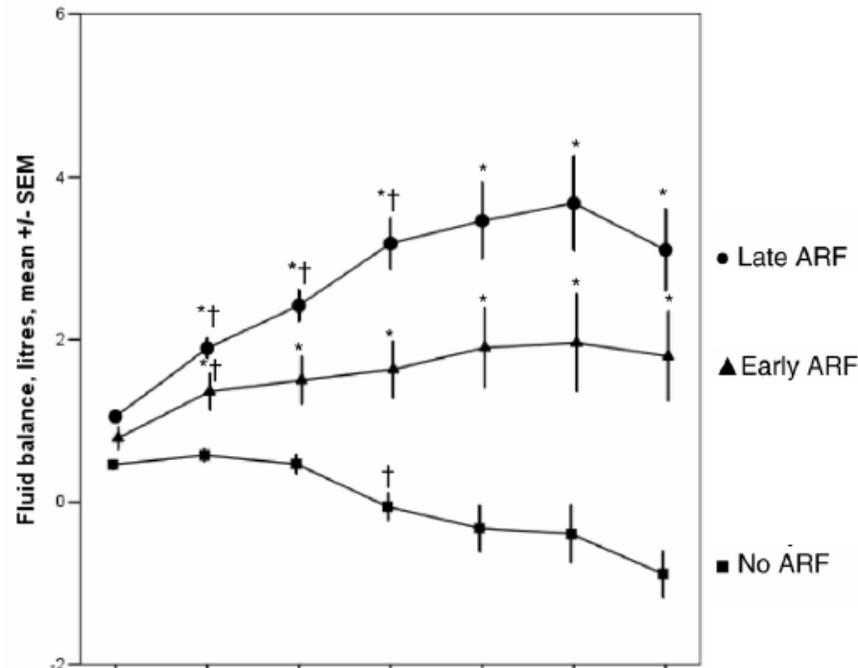
Fig. 5 Mortality rate by fluid accumulation in 3 days relative to baseline weight in patients with acute kidney injury. *P* value is the result of comparing the neighboring groups. **P* < 0.05; ***P* < 0.001

Timing de début



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

Critical Care 2008, 12:R74



ARF: creat >350µmol/L or UO <500ml/d

Early RRT: ≤ 48h after admission

Late RRT: > 48h after admission

Table 5

Characteristics of patients with acute renal failure, stratified by time of initiation of renal replacement therapy (RRT)

Characteristic	Early RRT n = 213	Late RRT n = 65	P value
ICU mortality, number (percentage)	84 (39.4)	40 (61.5)	<0.01
60-day mortality, number (percentage)	94 (44.8)	42 (64.6)	<0.01

Data represent mean ± standard deviation, number (percentage), or median (interquartile range). ICU, intensive care unit; SAPS II, Simplified Acute Physiology Score II; SOFA, sequential organ failure assessment.

Timing de début



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

Intensive Care Med (2016) 42:1155–1158
DOI 10.1007/s00134-015-4186-2

WHAT'S NEW IN INTENSIVE CARE



Miet Schetz
Lui G. Forni
Michael Joannidis

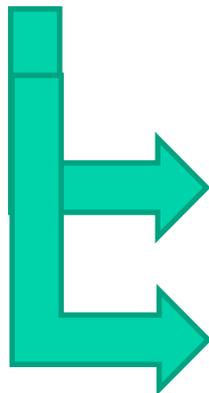
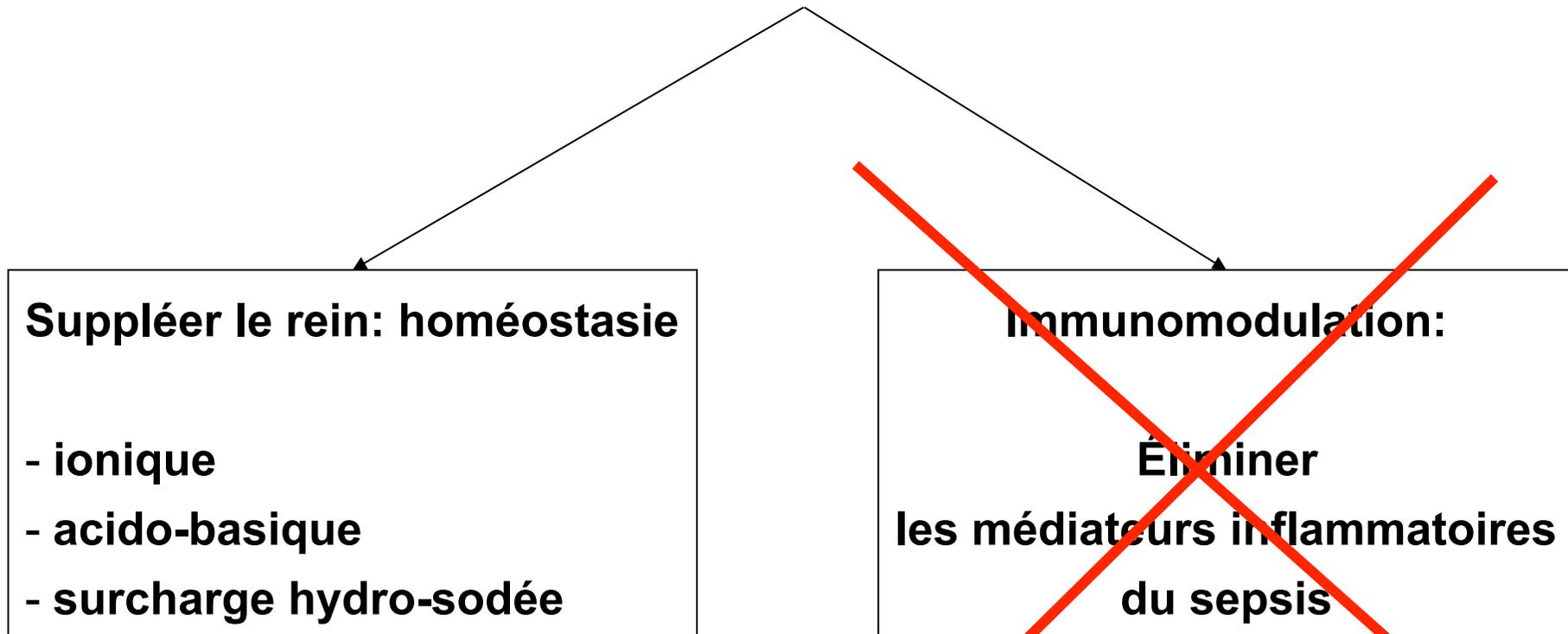
Does this patient with AKI need RRT?

failure) [13]. Besides an assessment of the reversibility of kidney dysfunction, the tolerance to fluid overload (mainly cardiac and respiratory acute illness and comorbidity) may therefore become an important factor in the decision to start RRT.

ICU mortality, number (percentage)	84 (39.4)	40 (61.5)	<0.01
60-day mortality, number (percentage)	94 (44.8)	42 (64.6)	<0.01

Data represent mean \pm standard deviation, number (percentage), or median (interquartile range). ICU, intensive care unit; SAPS II, Simplified Acute Physiology Score II; SOFA, sequential organ failure assessment.

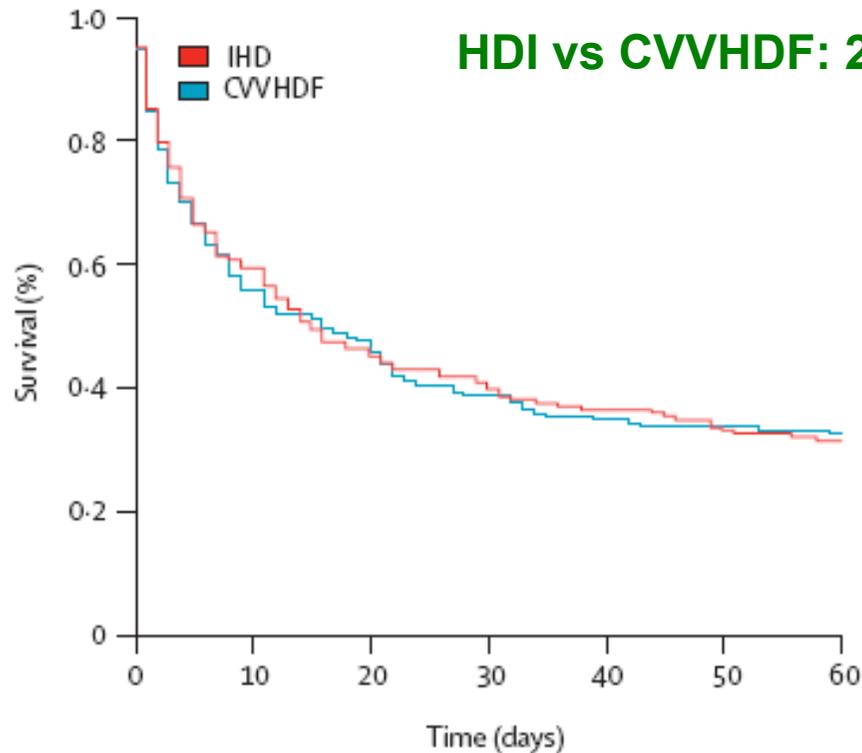
Objectifs de l'EER



Quand: désordres métaboliques sévères, prise de poids incontrôlable. Précocement n'apporte rien

Comment ??

Quelle mode ?



HDI: 69% sepsis
CVVHDF: 56% sepsis

	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

Data are number (percentage). *All hypotensive episodes were recorded from initiation until end of renal replacement therapy. Hypotension means at least one hypotensive episode during follow-up. †Bleeding events were reported only when transfusion was needed.

→ HDI = CVVHDF

Vinsonneau, lancet, 06

Quelle dose ?

The New England Journal of Medicine

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JANUARY 31, 2002

H Schiffi

DAILY HEMODIALYSIS AND THE OUTCOME OF ACUTE RENAL FAILURE

CHARACTERISTIC	ALTERNATE-DAY HEMODIALYSIS	DAILY HEMODIALYSIS	
Duration of session (hr)	3.4±0.5	3.3±0.4	
Blood-flow rate (ml/min)	243±25	248±45	
Dose (K·t/V)†			
Prescribed	1.21±0.09	1.19±0.11	
Delivered	0.94±0.11†	0.92±0.16†	
Weekly delivered	3.0±0.6	5.8±0.4	
Mortality — no. (%)†	37 (46)	22 (28)	0.01
Resolution of acute renal failure — days	16±6	9±2	0.001

Lancet 2000; 355: 26–30

Effects of different doses in continuous veno-venous haemofiltration on outcomes of acute renal failure: a prospective randomised trial

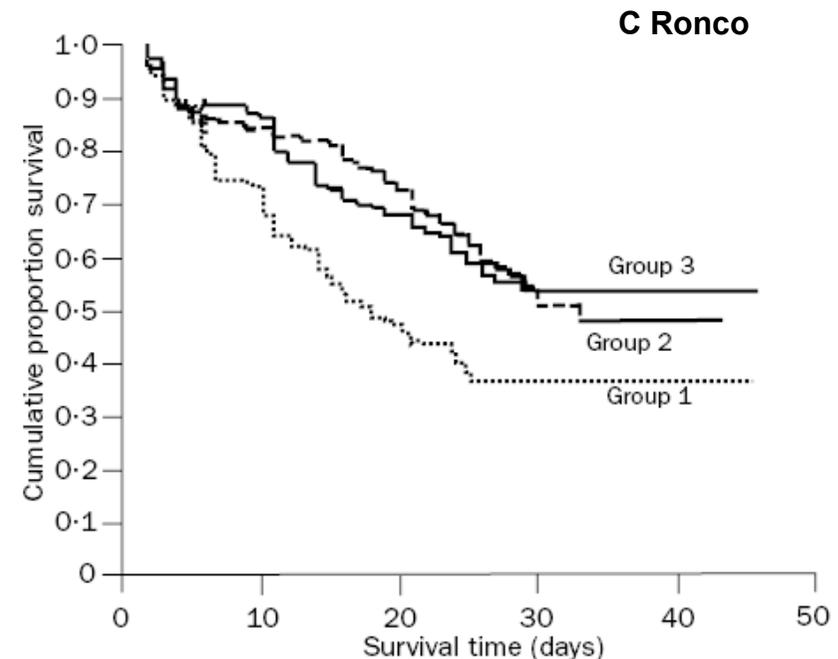


Figure 2: Kaplan Meier estimation of survival rates in the three groups

HDI / j > HDI / 48h

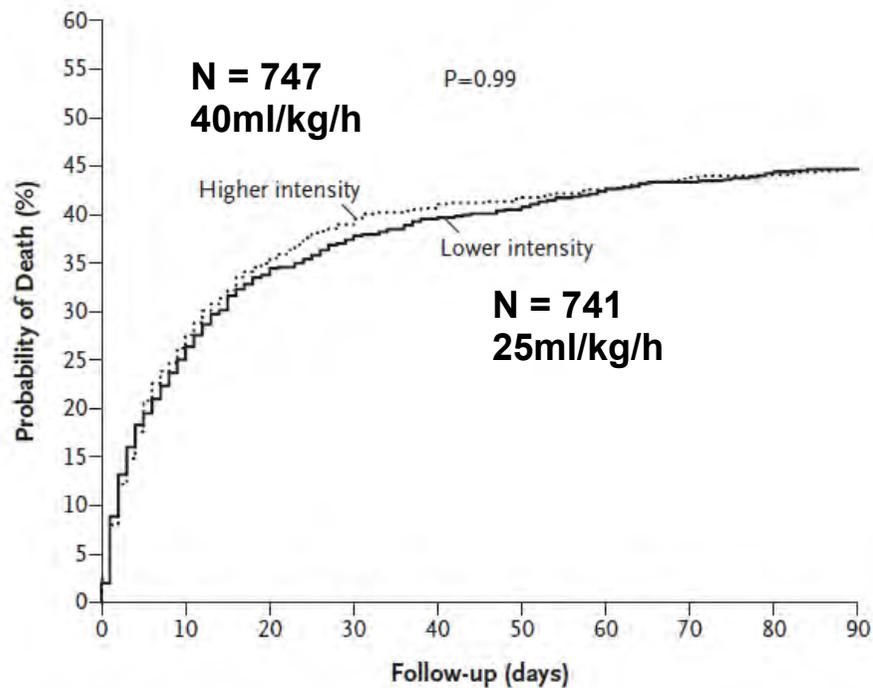
UF 45 = 35 > 20ml/kg/h

Quelle dose ?

Intensity of Continuous Renal-Replacement Therapy in Critically Ill Patients

N Engl J Med 2009;361:1627-38.

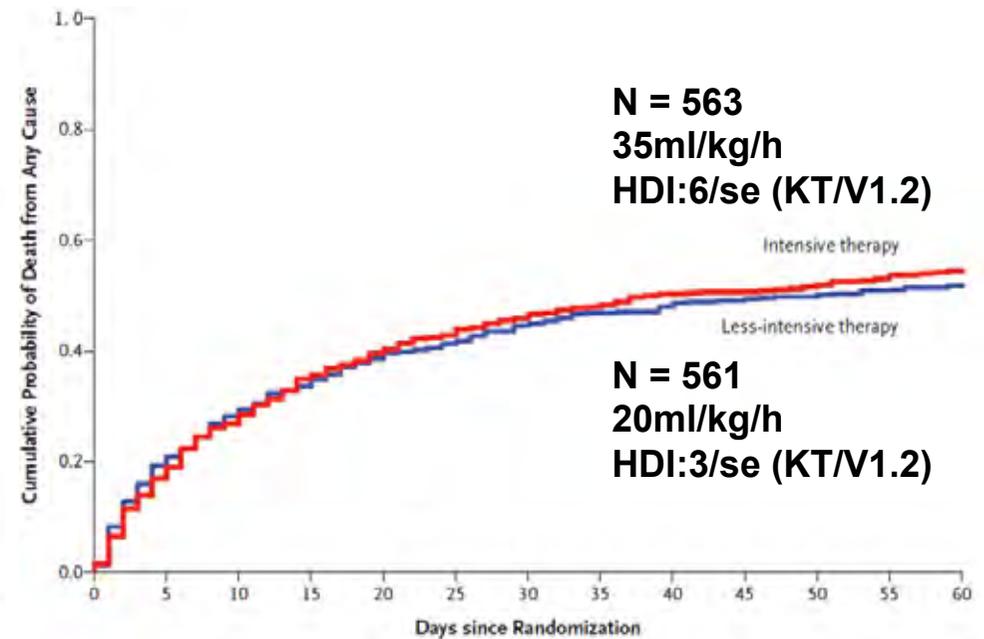
The RENAL Replacement Therapy Study Investigators*



Intensity of Renal Support in Critically Ill Patients with Acute Kidney Injury

N Engl J Med 2008;359.

The VA/NIH Acute Renal Failure Trial Network*



Quelle dose ?

The RENAL Replacement Therapy Study Investigators*

Prespecified Subgroup	Higher Intensity (N=721)	Lower Intensity (N=743)	Odds Ratio (95% CI)	
	<i>no. of deaths/no. of patients (%)</i>			
Patients with criteria for sepsis				
Yes	168/359 (46.8)	186/363 (51.2)		0.84 (0.62–1.12)
No	154/362 (42.5)	145/379 (38.3)		1.19 (0.89–1.60)

The VA/NIH Acute Renal Failure Trial Network*

Baseline Characteristic	No. of Patients	Intensive Therapy	Less-Intensive Therapy	Odds Ratio for Death at 60 Days (95% CI)	P Value for Interaction
Sepsis					0.36
No	416	47.8	49.8	0.94 (0.63–1.41)	
Yes	708	57.0	52.6	1.19 (0.88–1.62)	

0.5 1.0 1.5 2.0 2.5
 ← Intensive Therapy Better Less-Intensive Therapy Better →

Quelle dose ?

The VA/NIH Acute Renal Failure Trial Network*

Ronco, lancet, 00

Characteristics	Group 1 (n=146)	Group 2 (n=139)	Group 3 (n=140)
Clinical characteristics			
Presence of sepsis	20 (14%)	17 (12%)	15 (11%)
Mean (SD) blood urea nitrogen (mmol/L)	18.2 (4.3)	17.9 (3.9)	19.3 (4.3)
Mean (SD) serum creatinine (μmol/L)	309.4 (132.6)	327.1 (141.4)	318.2 (185.6)
Mean (SD) APACHE II score	22 (3)†	24 (4)*	22 (4)
Mean prescribed ultrafiltration (L/24 h)	32.4 (5.3)	57.6 (7.1)	71.9 (9.2)

*p<0.017 group 1 vs group 2. †p<0.017 group 2 vs group 3.

	Group 1	Group 2	Group 3
Mean (SD) delivered ultrafiltration (L/24 h)	30.9 (6.2)	55.7 (8.2)	68.2 (9.3)
Mean (SD) effective blood flow (mL/min)	145 (14)	171 (20)	207 (27)
Mean (SD) duration of replacement treatment (days)	11 (6)	13 (8)	12 (7)
Bleeding	5%	6%	4%
Repeated filter clotting	3%	2%	2%
Vascular-access malfunction	10%	11%	12%
Fluid-balance errors	4%	6%	7%

NEJM 08

Intensive Strategy (N = 563) vs Less-Intensive Strategy (N = 561)

CVVH

Effluent flow — ml/kg/hr

Prescribed	36.2±3.8	21.5±4.3
Delivered	35.8±6.4	22.0±6.1

Kt/V_{urea} HDI

First treatment	1.13±0.31	1.13±0.32
Subsequent treatments	1.32±0.37	1.31±0.33
Average value ≥1.2	199/297 (67.0)	184/266 (69.2)

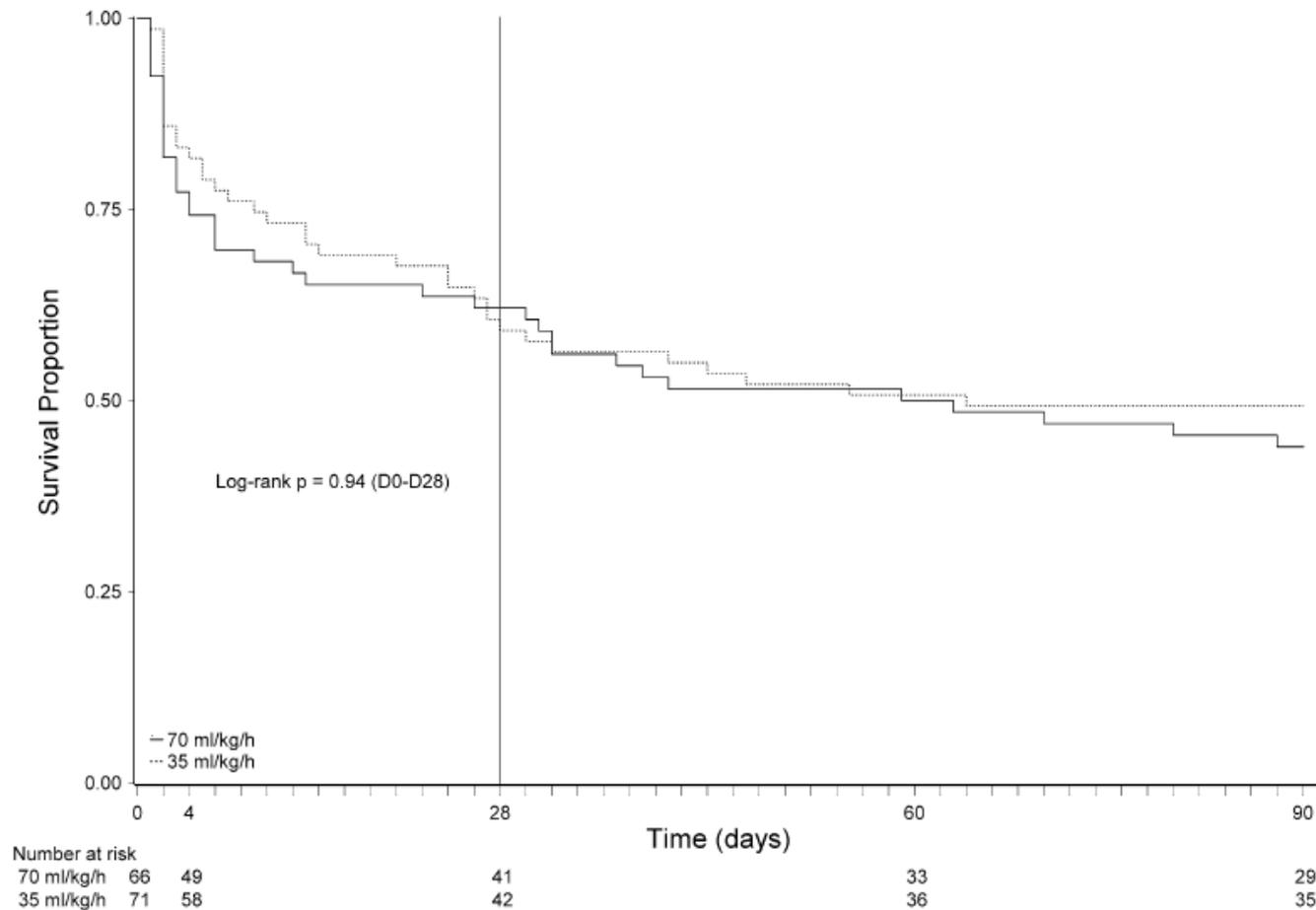
dose prescrite ≠ délivrée

dose prescrite = délivrée

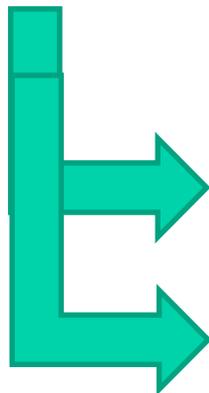
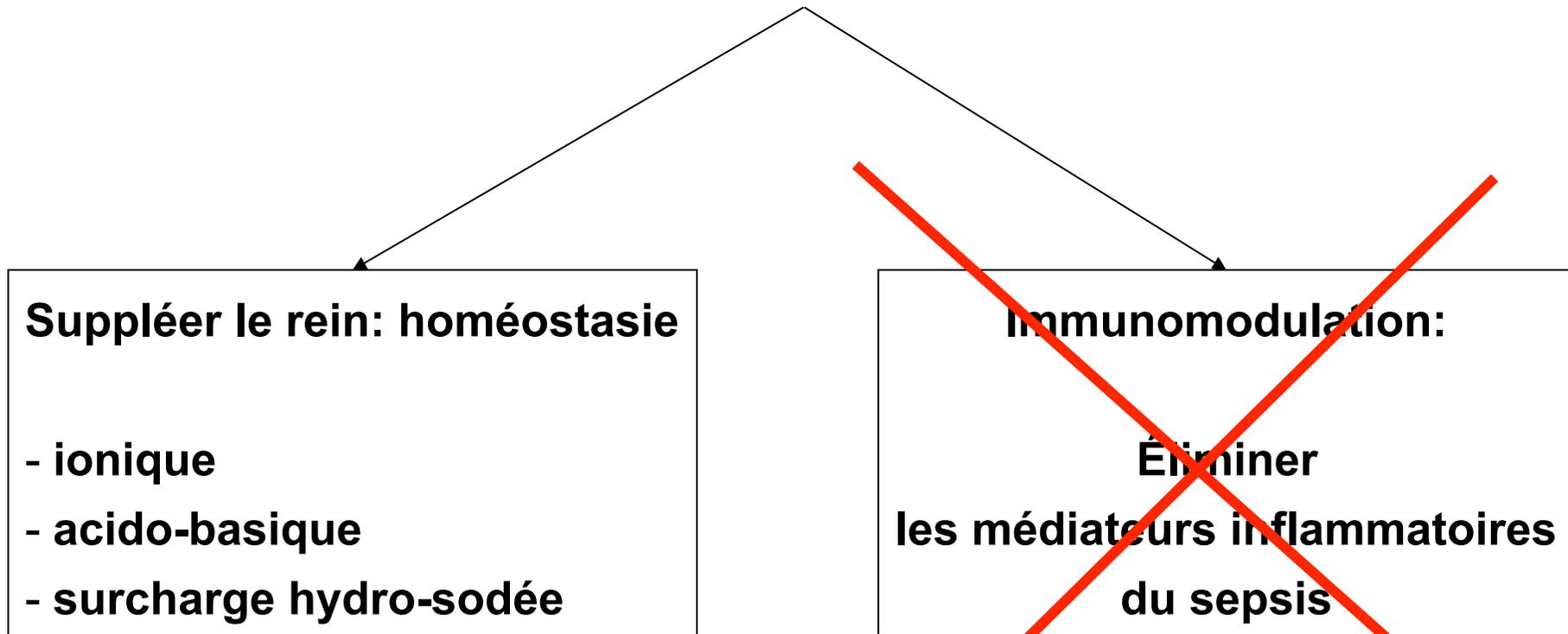
CVVH Haut volume ?

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

Intensive Care Med (2013) 39:1535–1546
DOI 10.1007/s00134-013-2967-z



Objectifs de l'EER



Quand: désordres métaboliques sévères, prise de poids incontrôlable. Précocement n'apporte rien

Comment: CRRT (20-30ml/kg/h) = HDI (KT/V 1,2 x3/sem)

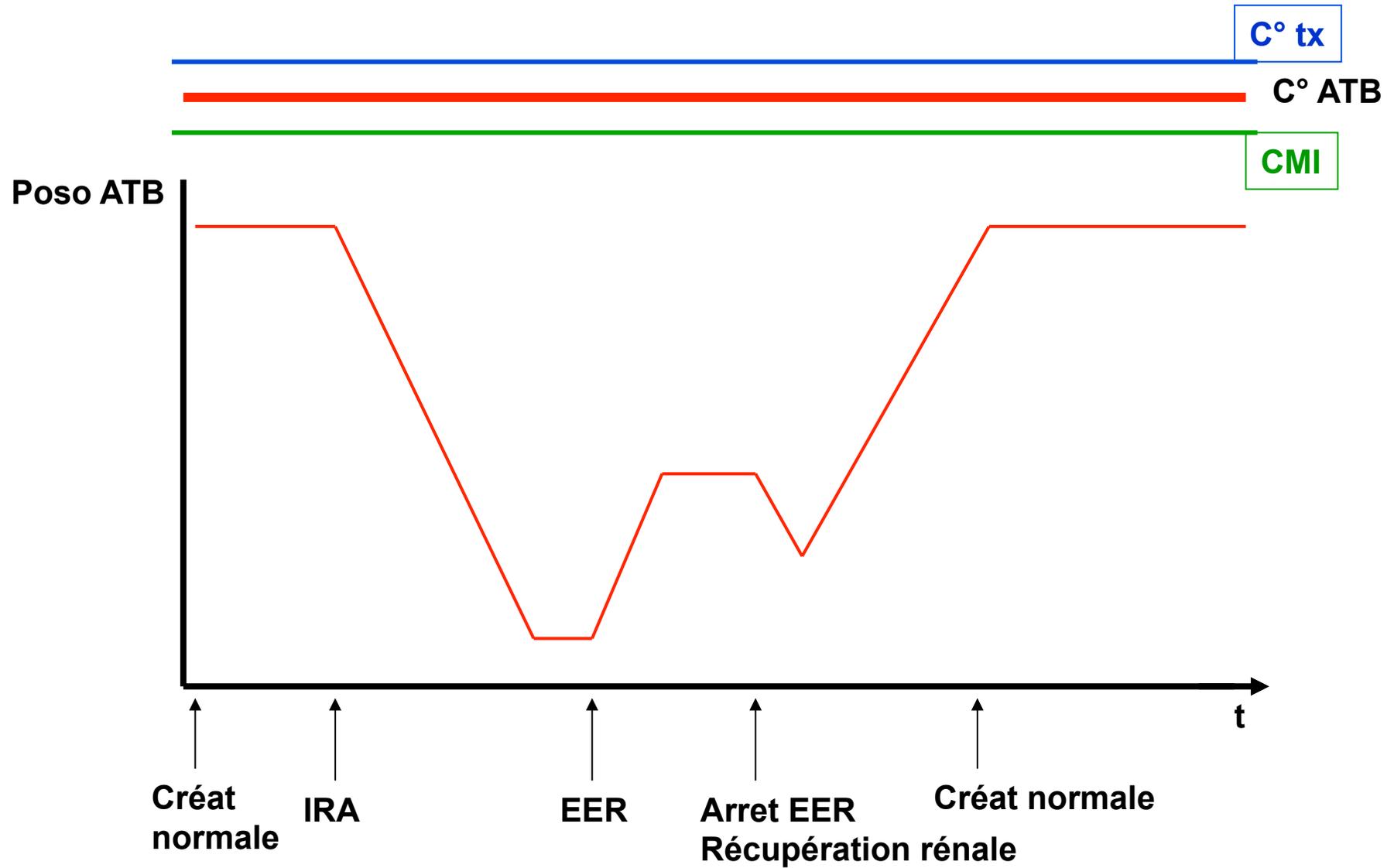
Votre objectif.....

C° tx

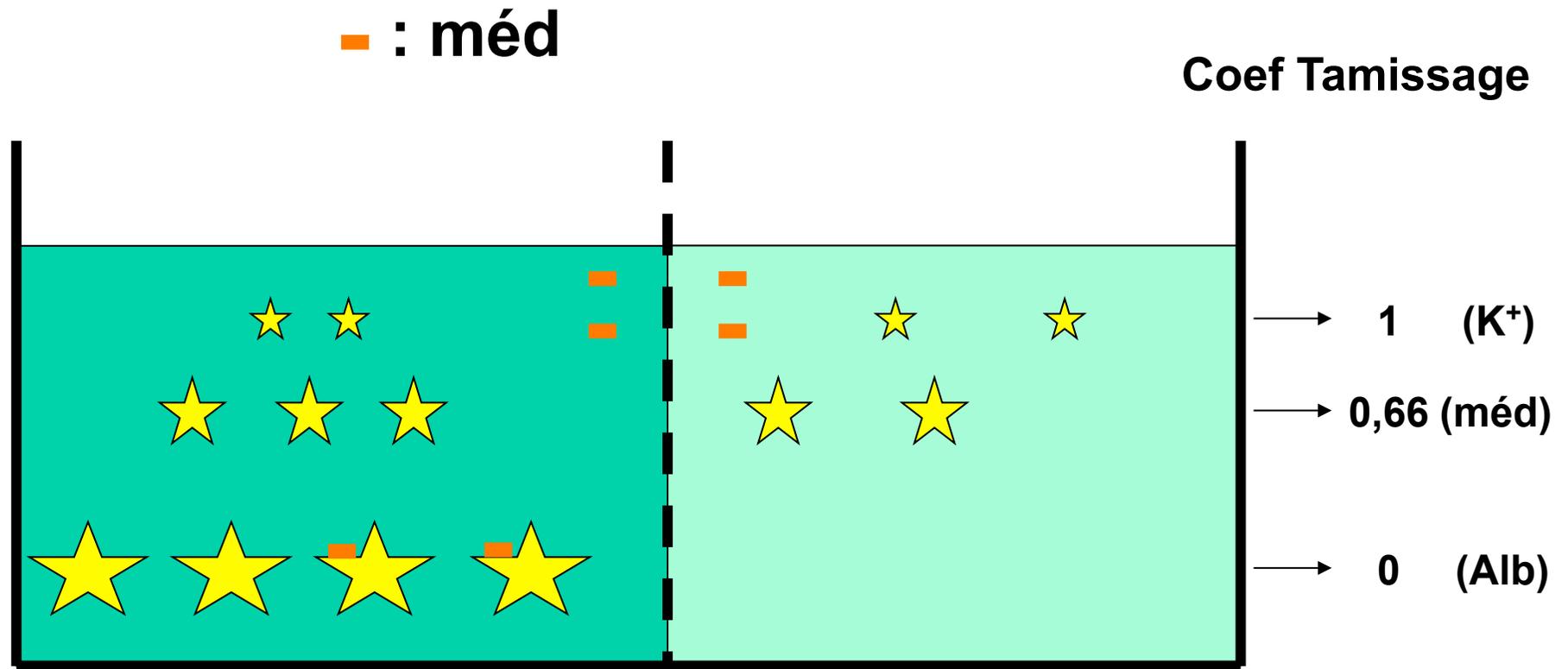
C° ATB

CMI

Votre objectif.....



Epuration des médicaments ?



Médicament lié à l'albumine n'est pas épuré

Epuration des médicaments ?

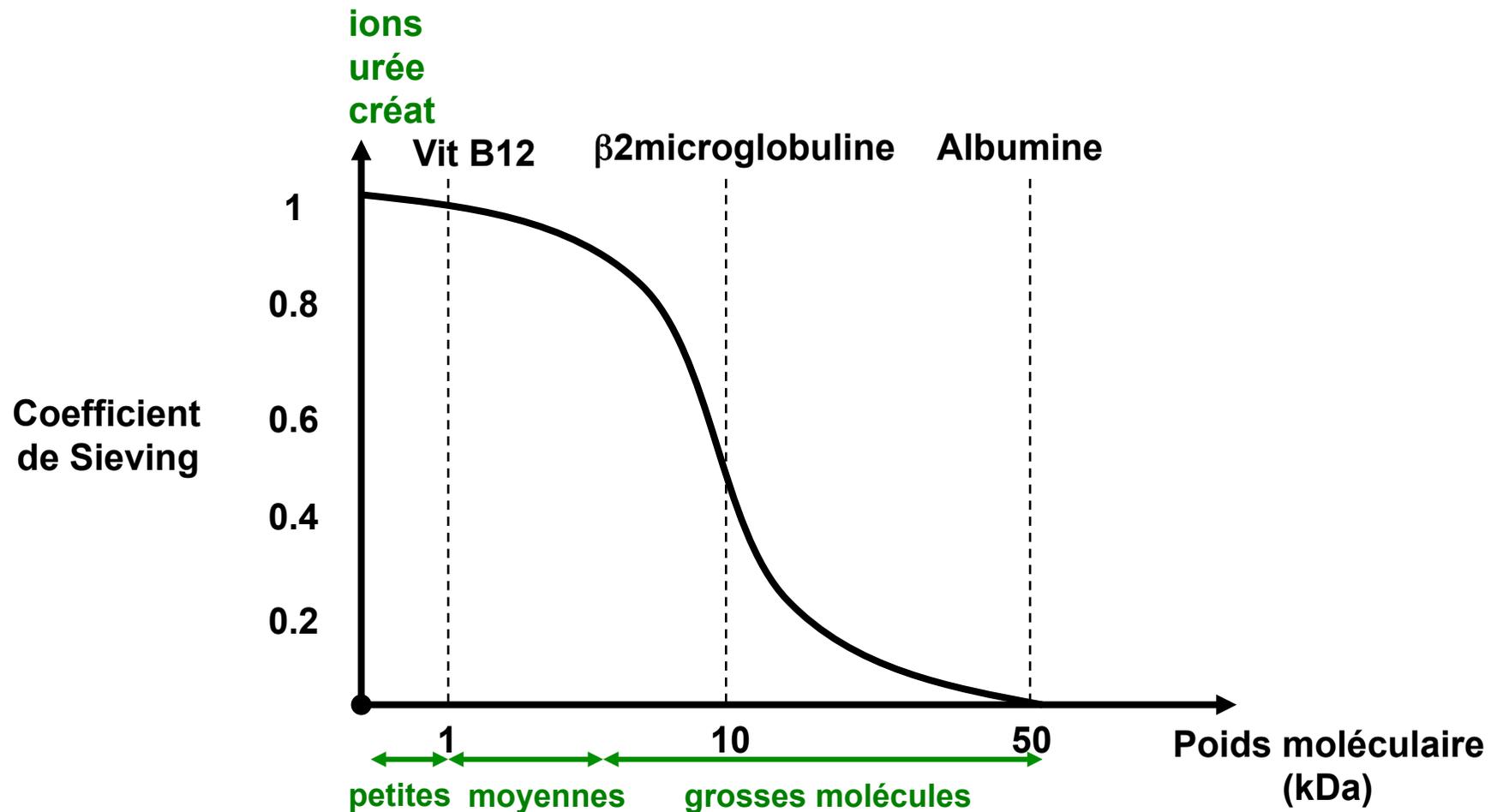
charge ionique

Albumine = charges négatives

	charge	effet
Gentamycine	Cationique (+)	Tranfert légèrement <u>inférieur</u> à celui attendu
Céphalosporines	Anionique (-)	Tranfert légèrement <u>supérieur</u> à celui attendu

Epuration des médicaments ?

PM + F_L + charge ionique → Coef Sieving



$$\text{Coefficient de Sieving} = \frac{[]_{UF}}{[]_{PLASMA}}$$

Épuration des médicaments ?

selon technique d'EER

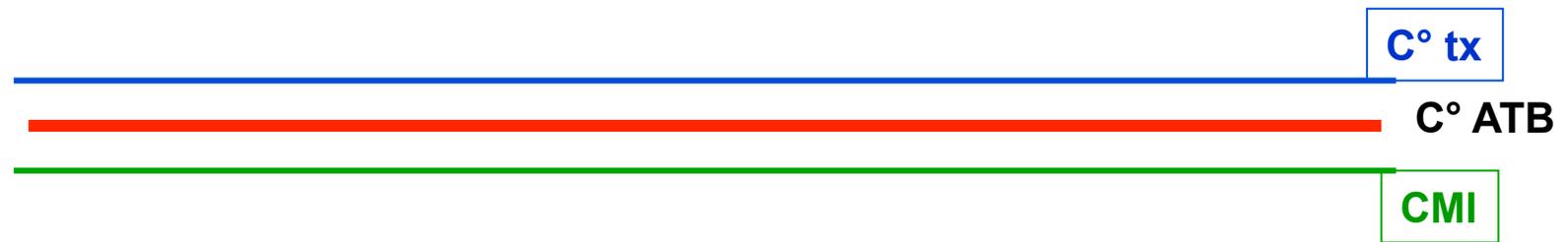
Hémodialyse: 200-300 ml/min (= Q_{sg})

Hémofiltration: 20-50 ml/kg/h (= Q_{UF} , patient 80kg, 30ml/kg/h: 40ml/min)

Hémofiltration à haut volume: 100ml/kg/h (= Q_{UF} : 130ml/min)

→ 5h d'HDI = 30h d'HF = 10h d'HFHV

Votre objectif.....



- **EER épure les petits médicaments non liés à l'albumine**
- **HDI: injection médicament après séance**
- **CVVH: injection n'importe quand..**
- **Posologie adaptée.....**

Merci de votre attention