EER quoi de neuf en 2013 ?

EUROPIARMAT 2013

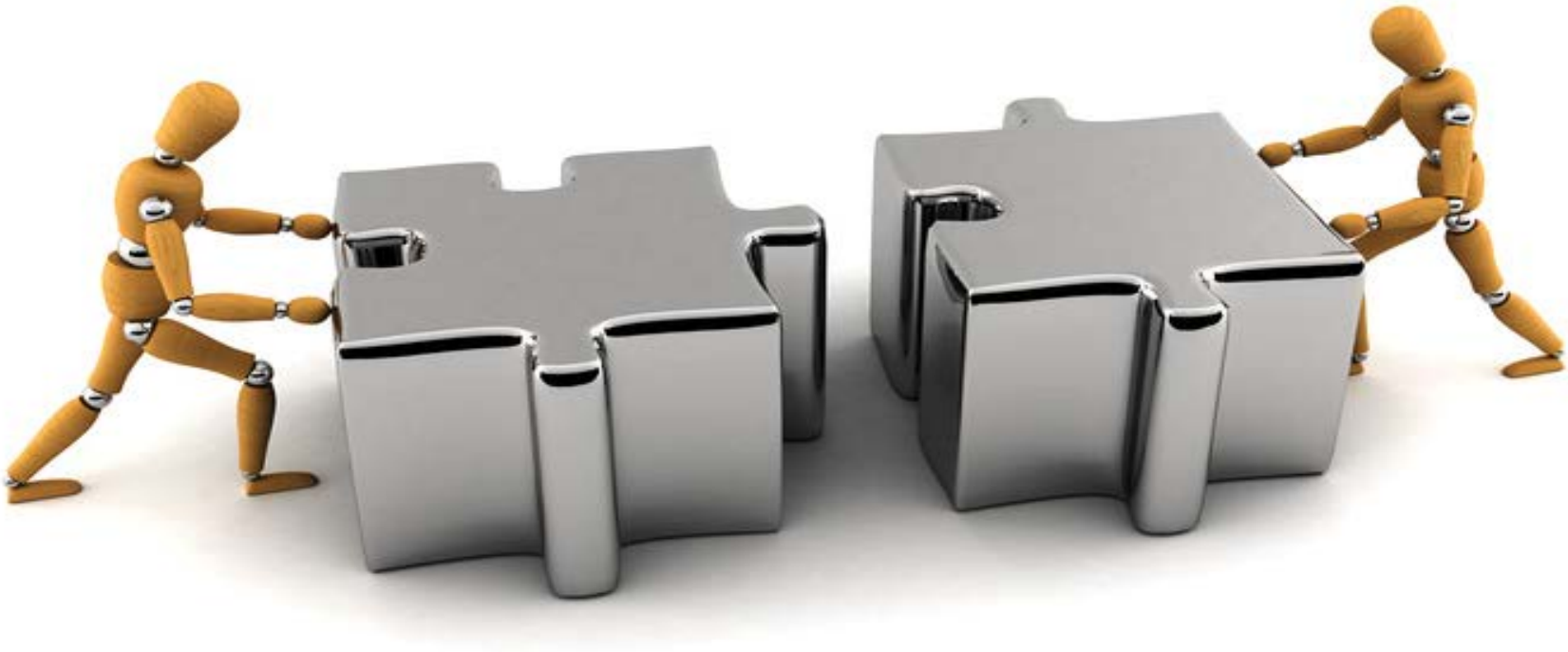
O. JOANNES-BOYAU

SAR II, CHU Bordeaux

Olivier.joannes-boyau@chu-bordeaux.fr

Modality of RRT for Patients with AKI

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



Modality of RRT for Patients with AKI

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

Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008*

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Jean M. Carlet, MD; Julian Bion, MD; Margaret M. Parker, MD; Roman Jaeschke, MD;

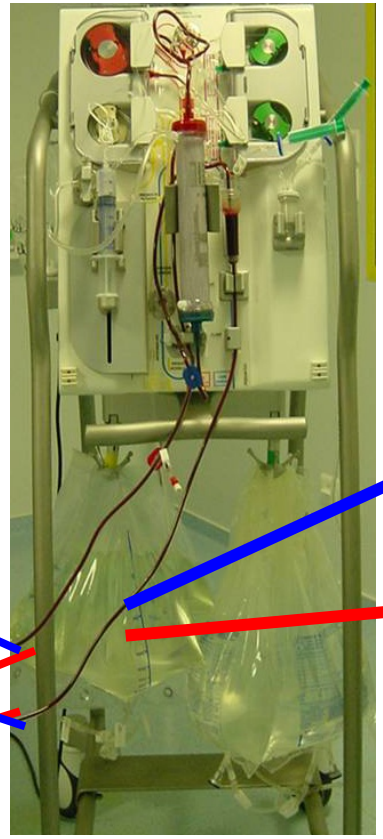
Crit Care Med 2008

D. Renal Replacement

1. We suggest that continuous renal replacement therapies and intermittent hemodialysis are equivalent in patients with severe sepsis and acute renal failure (grade 2B).
2. We suggest the use of continuous therapies to facilitate management of fluid balance in hemodynamically unstable septic patients (grade 2D).

Epuration dans le sepsis ?

Grootendorst AF. *J Crit Care* 1993



Control

Septiques

Ultrafiltrat

Ultrafiltrat

Pas d'effet

SVRi

+ CO

Sepsis like

Impact of High Volume Hemofiltration on Hemodynamic Disturbance and Outcome during Septic Shock

Olivier Joannes-Boyau, Stephane Rapaport, Romain Bazin, Catherine Fleureau, and Gerard Janvier

ASAIO Journal 2004;

- Étude pilote, prospective, sur 1 an
- 24 patients en état de choc septique
- Inclus selon les critères de Bone
- Traités par HVHF durant 96 h à 50 $ml.kg^{-1}.h^{-1}$
- Etude de l'évolution des paramètres :
  - hémodynamiques, biologiques et des doses de noradrénaline
- Statistiques
  - Test ANOVA d'analyse de variance pour mesures répétées
  - test de sheffé
  - La mortalité observée est comparée à la mortalité prédite par les scores de SOFA, LOD et MODS.

Impact of High Volume Hemofiltration on Hemodynamic Disturbance and Outcome during Septic Shock

Olivier Joannes-Boyau, Stephane Rapaport, Romain Bazin, Catherine Fleureau, and Gerard Janvier

ASAIO Journal 2004;

- L 'hémofiltration à haut volume participe à :
  - Une amélioration rapide des fonctions hémodynamiques
  - Une diminution significative des doses de noradrénaline

Mortalité observée 46%

VS

Mortalité prédite 70%

(p<0,075)

Nicolas Boussekey
Arnaud Chiche
Karine Faure
Patrick Devos
Benoit Guery
Thibaud d'Escrivan
Hugues Georges
Olivier Leroy

A pilot randomized study comparing high and low volume hemofiltration on vasopressor use in septic shock

Intensive Care Med (2008) 34:1646–1653

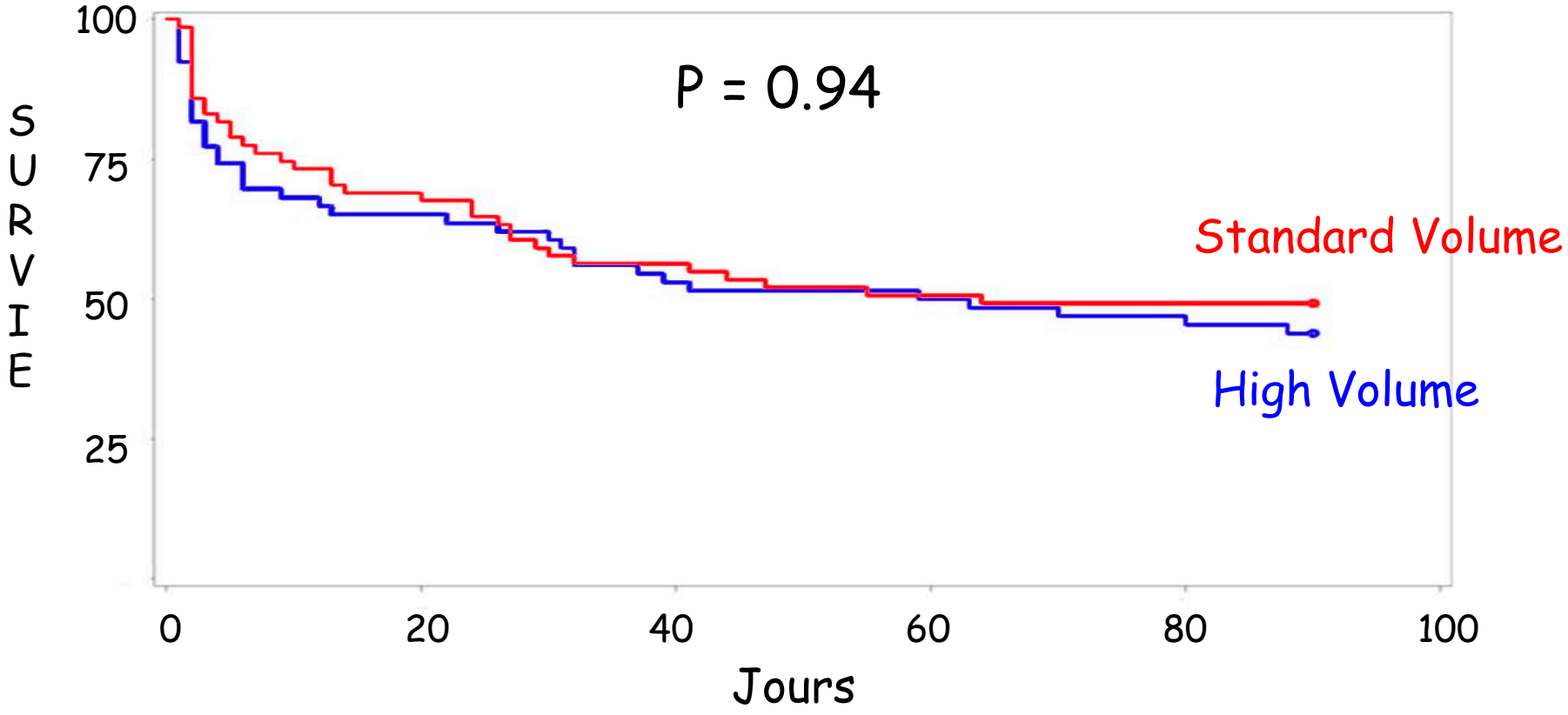
- 19 patients Randomisés
- 35 ml/kg/h Vs 65 ml/kg/h pdt 4 jours
- Mortalité globale à **J28 = 47%**
- Mortalité spécifique : LVH = 50% **vs HVH = 44%**

Time (h)	LVHF		HVHF	
	Non-responders $n = 6$	Responders $n = 4$	Non-responder $n = 1$	Responders $n = 8$
0	0.99 (0.54–1.17)	0.38 (0.26–0.44)	2.38	1.01 (0.3–1.3)
6	0.94 (0.78–1.5)	0.28 (0.17–0.39)	1.19	0.45 (0.18–0.8)
12	0.81 (0.43–1.69)	0.2 (0.1–0.3)	0.95	0.27 (0.07–0.43)
18	0.73 (0.35–2.66)	0.04 (0.01–0.1)	0.83	0.19 (0.02–0.37)
24	0.56 (0.27–2.77)	0 (0–0.05)	0.95	0.06 (0–0.21)

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

Olivier Joannes-Boyau
Patrick M. Honoré
Paul Perez
Sean M. Bagshaw
Hubert Grand
Jean-Luc Canivet
Antoine Dewitte

Intensive Care Med 2013



« HEROIC study »

360 patients en post-chirurgie cardiaque

Dose catécholamine Nad ou Adre

Randomisation sous 24h

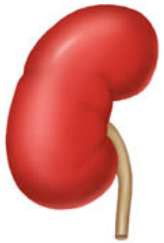
35 ml/kg/h

80 ml/kg/h

Mortality

D28

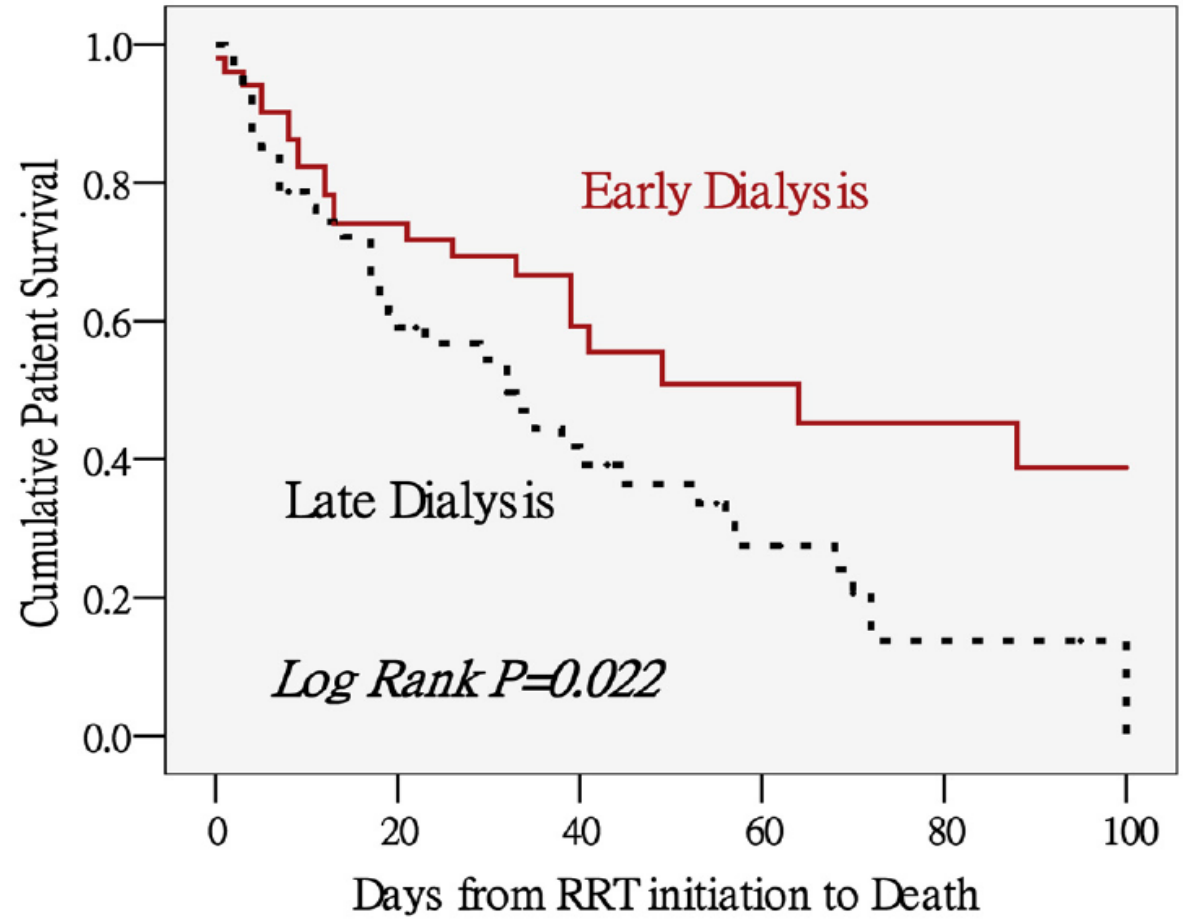
D90

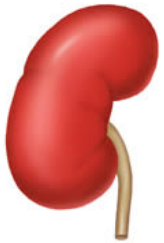


Late initiation of renal replacement therapy is associated with worse outcomes in acute kidney injury after major abdominal surgery

Chih-Chung Shiao[1], Vin-Cent Wu[2], Wen-Yi Li[3], Yu-Feng Lin[2], Fu-Chang Hu[4], Guang-Huar Young[5],

Critical Care 2009, **13**:R171

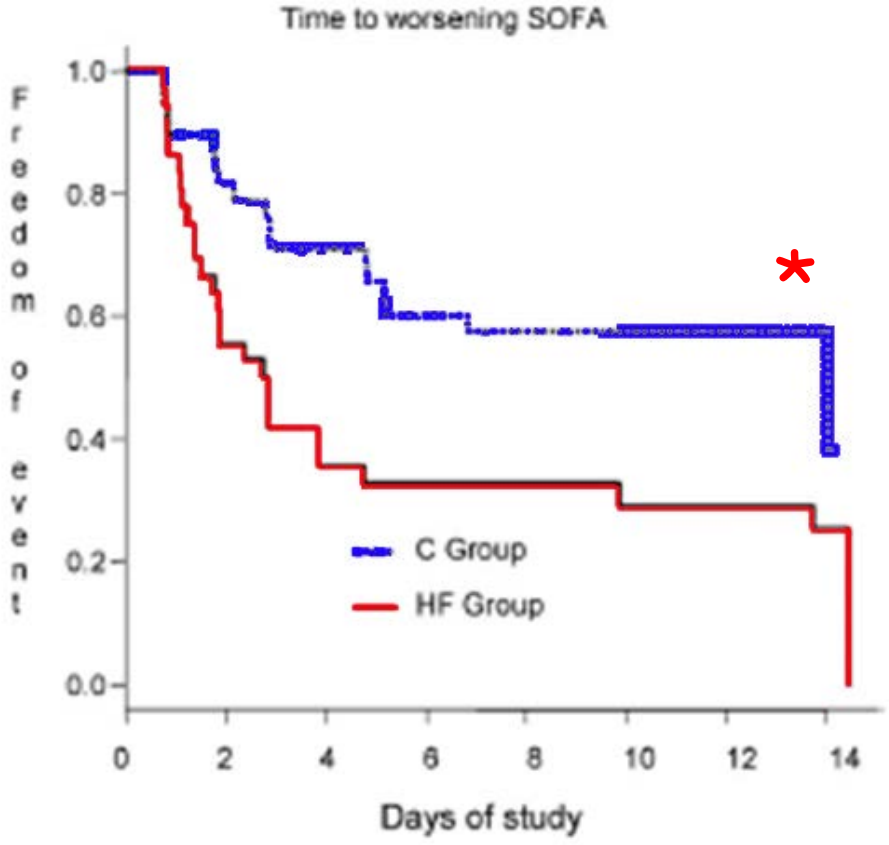


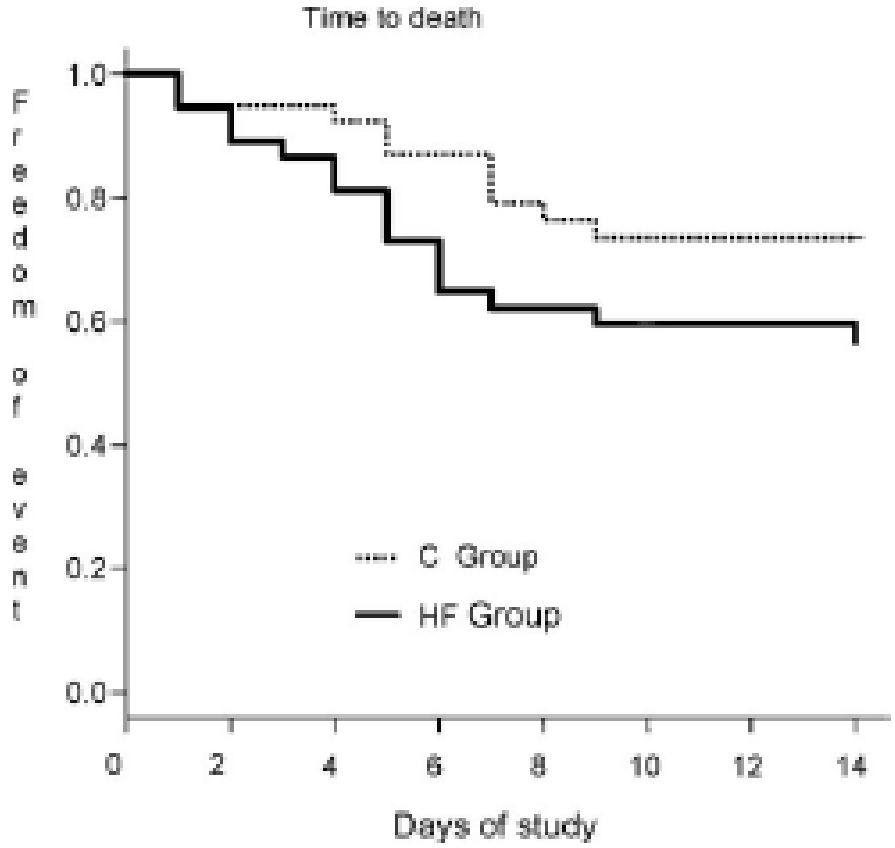


Impact of continuous venovenous hemofiltration on organ failure during the early phase of severe sepsis: A randomized controlled trial*

Didier Payen, MD, PhD; Joaquim Mateo, MD; Jean Marc Cavaillon, PhD; François Fraisse, MD; Christian Floriot, MD; Eric Vicaut, MD, PhD; for the Hemofiltration and Sepsis Group of the Collège National de Réanimation et de Médecine d'Urgence des Hôpitaux extra-Universitaires

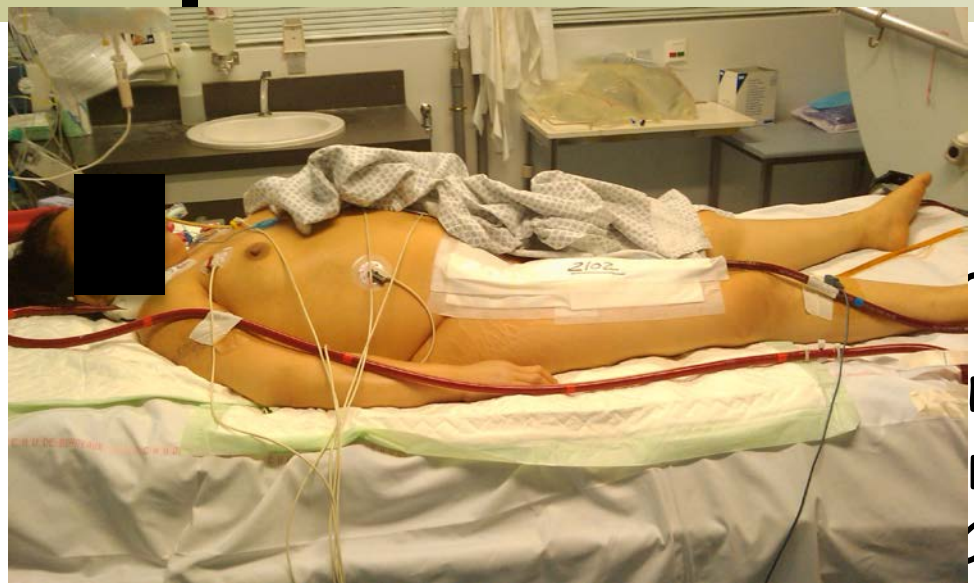
Crit Care Med 2009





Anticoagulation

Chapter 5.3: Anticoagulation



an increased
already receiv
ne following:

n *intermitten*
r low-molecula
C)

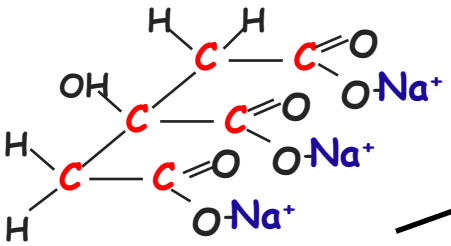
- ✓ 5.3.2.2: For anticoagulation in ***CRRT***, we s
citrate anticoagulation rather than hepar
not have contraindications for citrate. *(2*
- ✓ 5.3.2.3: For anticoagulation during ***CRRT*** in patients who have contraindications for citrate, we suggest using either UH or LMWH, rather than other anticoagulants. *(2C)*

Citrate, Calcium, Coagulation

Citrate = Chélateur du calcium

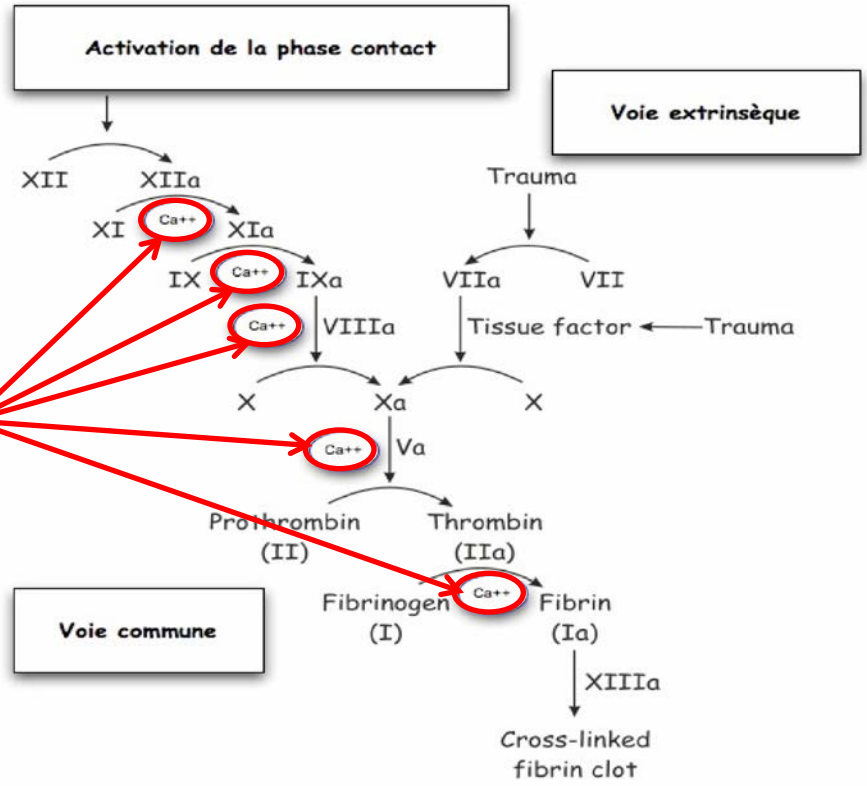
Hypocalcémi

Citrate trisodique



Ca^{2+}

Cascade de la coagulation

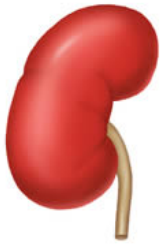


Calcium = cofacteur indispensable à:

- **Coagulation**
- **Activation leucocytes**
- **Voie alterne du complément**

et **Citrate = Chélateur du magnésium**

Hypomagnésémie => Supplémentation



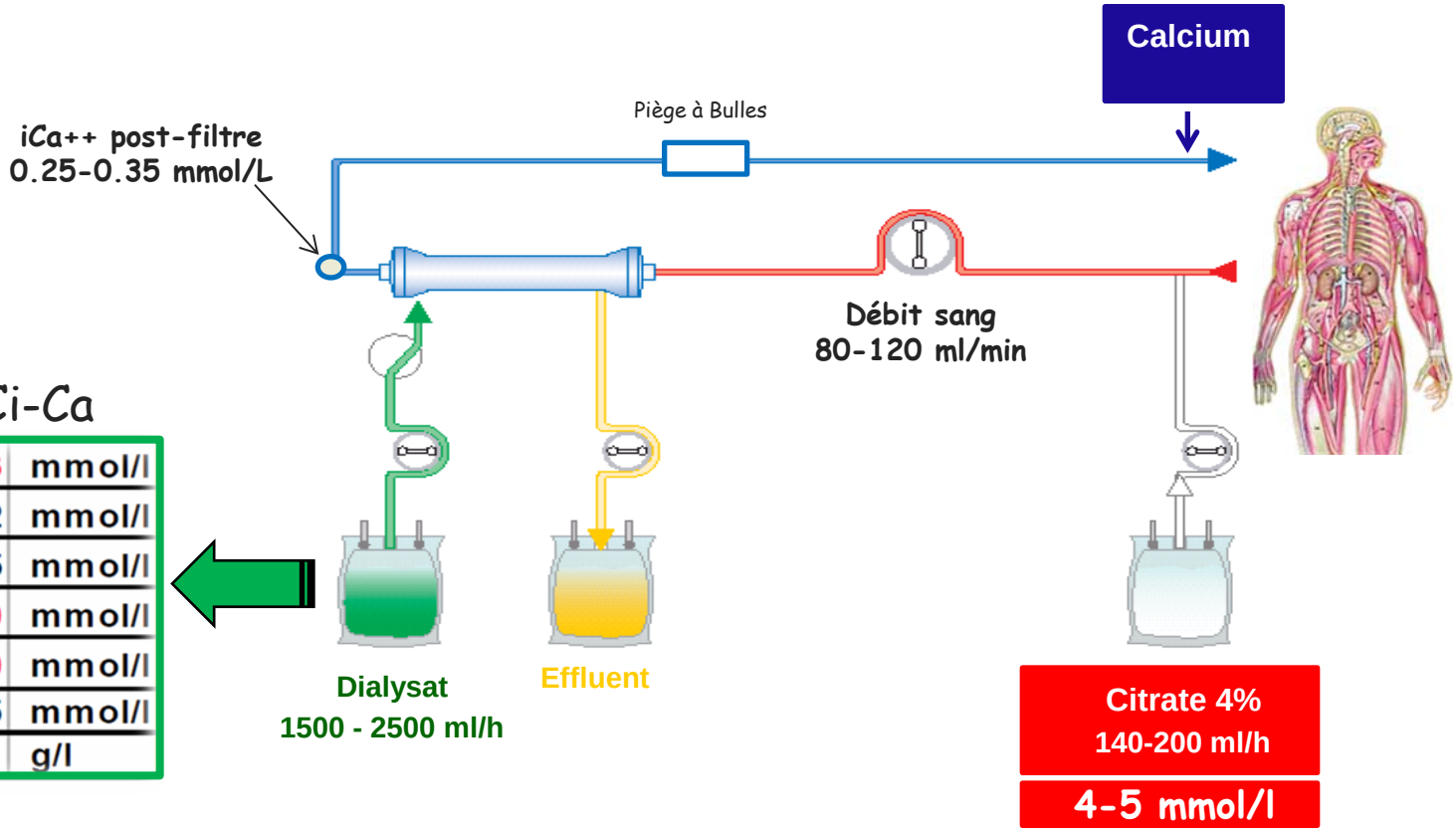
A safe citrate anticoagulation protocol with variable treatment efficacy and excellent control of the acid–base status*

Stanislao Morgera, MD; Michael Schneider, MD; Torsten Slowinski, MD; Ortrud Vargas-Hein, MD; Heidrun Zuckermann-Becker, MD; Harm Peters, MD; Detlef Kindgen-Milles, MD; Hans-Hellmut Neumayer, MD

Crit Care Med 2009; 37:2018–2024

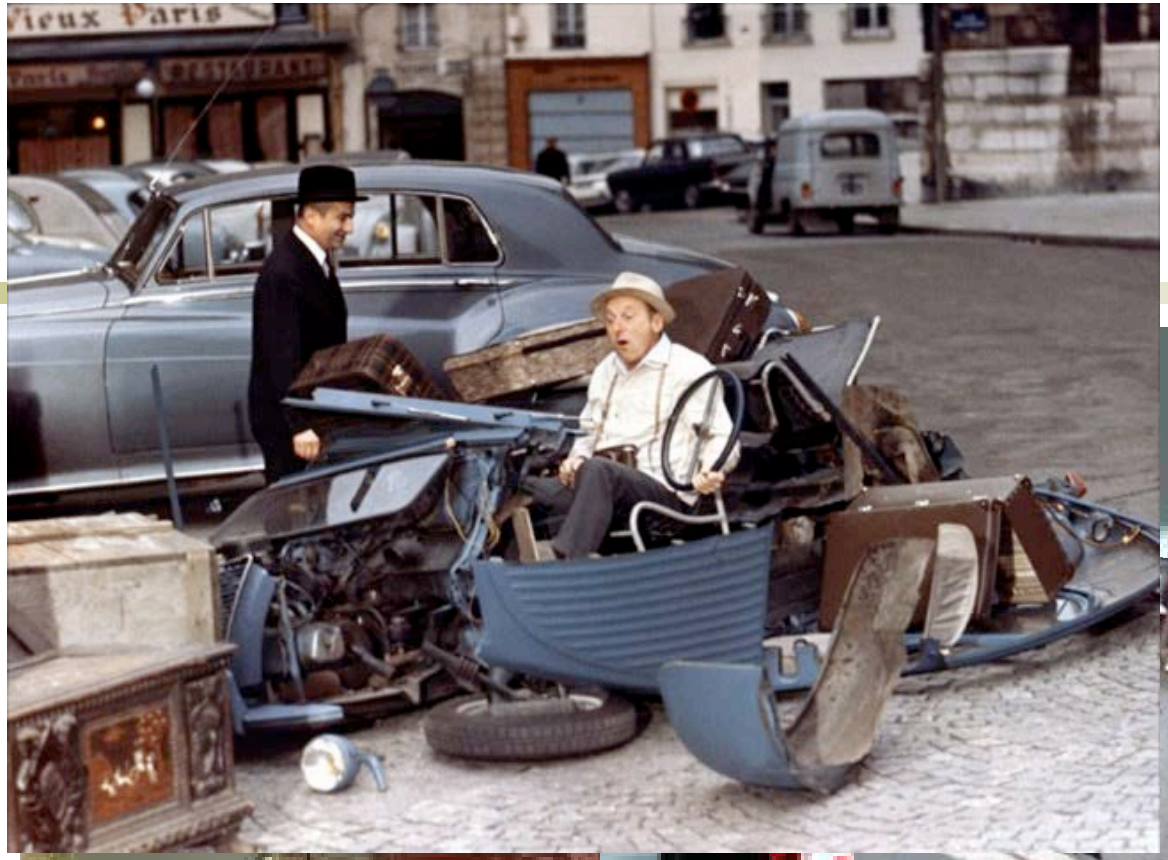
Utiliser en CVVHD

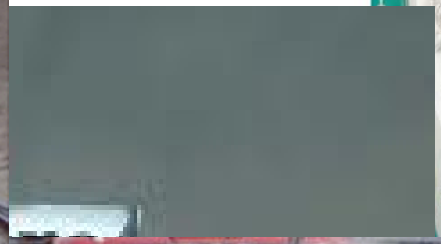
Citrate trisodique 4% : citrate 140 mmol/l, sodium 420 mmol/l



Dialysat Ci-Ca

Na^+	133	mmol/l
K^+	2	mmol/l
Mg^{++}	0.75	mmol/l
Ca^{++}	0	mmol/l
HCO_3^-	20	mmol/l
Cl	116.5	mmol/l
Glucose	1	g/l


Vieux Paris



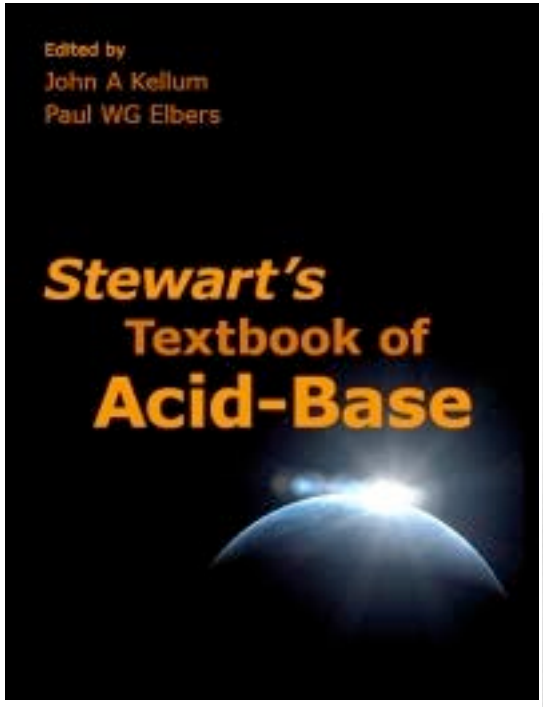

T10

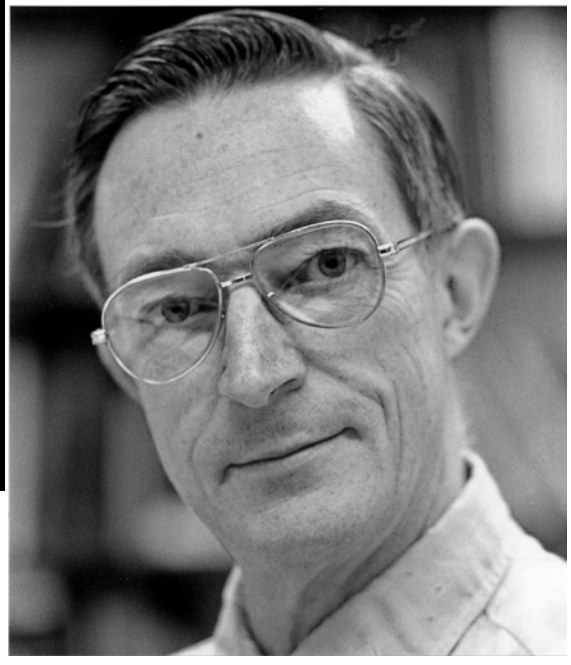
re ?


Mar oro
vodafone


BRIDGESTONE
NAVYBOOT
PETRONAS
M.SCHUMACHER
lmilch

Stewardt ?


Edited by
John A Kellum
Paul WG Elbers
Stewart's
Textbook of
Acid-Base



Efficacy and safety of regional citrate anticoagulation in critically ill patients undergoing continuous renal replacement therapy

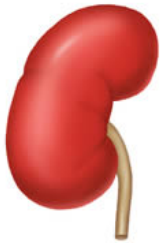
Zhongheng Zhang
Ni Hongying

Intensive Care Med (2012)

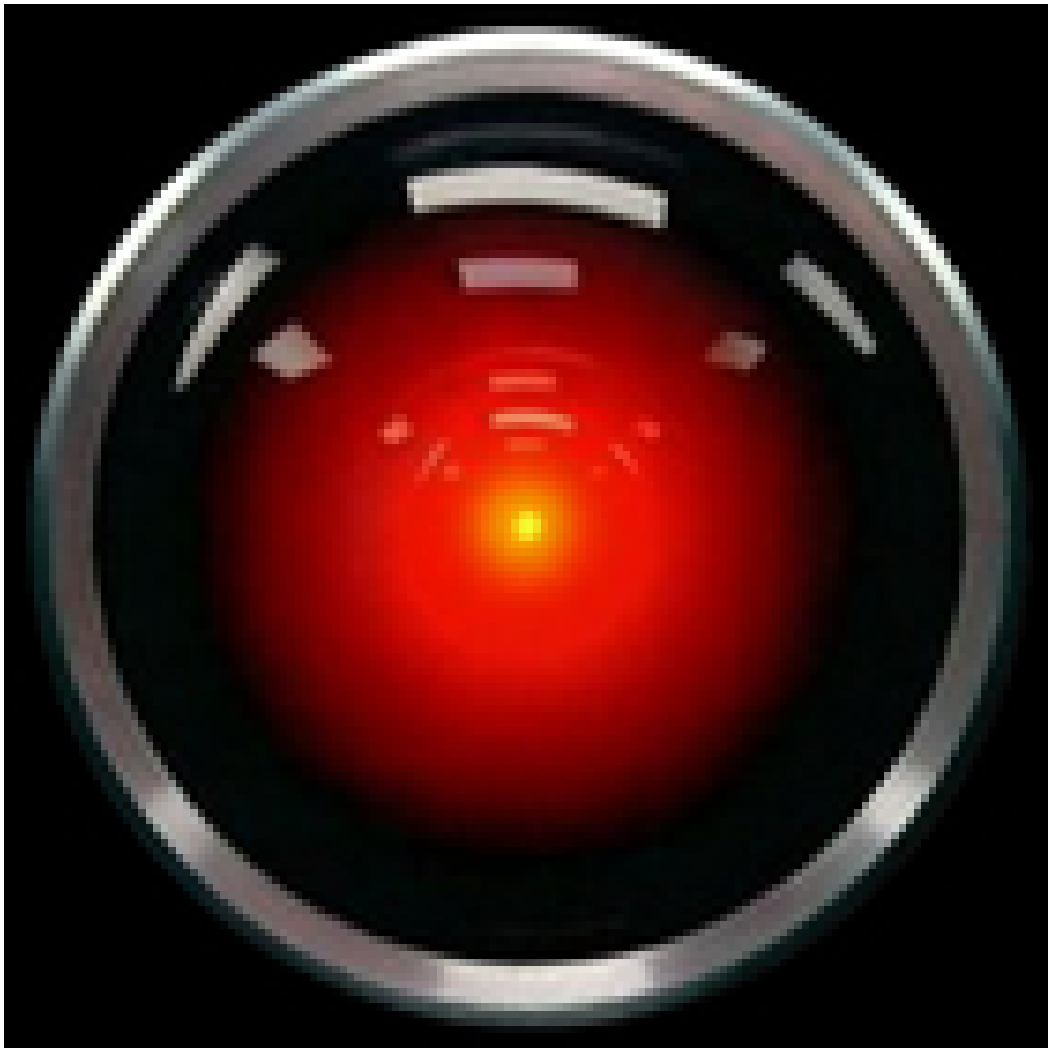
bleeding, and thus can be recommended for CRRT if and when metabolic monitoring is adequate and the protocol is followed. However, the safety of citrate in patients with liver failure cannot be concluded

Table 2 Outcome parameters and relevant definitions in individual studies

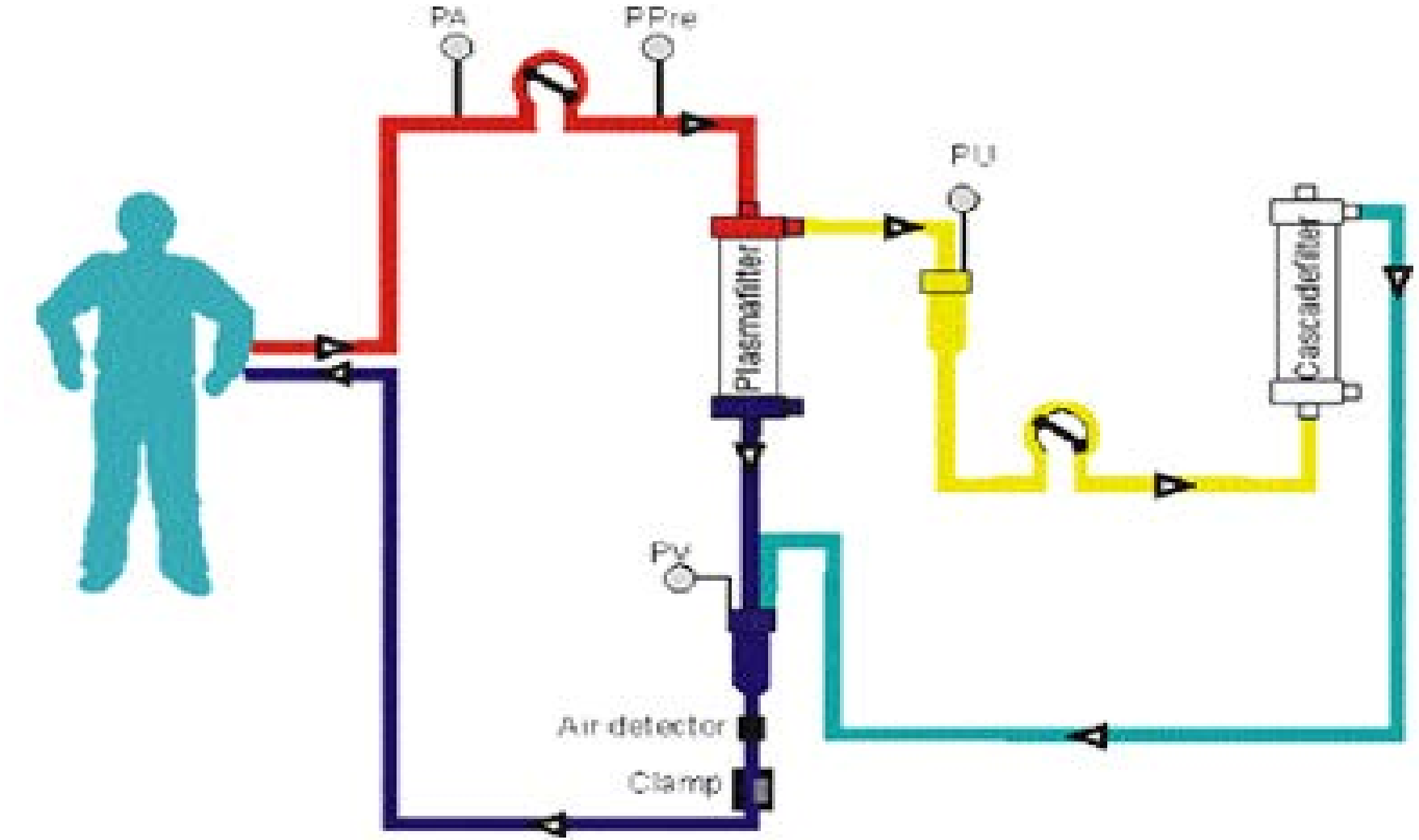
Study	Bleeding	Circuit life span (definition of filter clotting)	Mortality	Acid–base status	Sodium homeostasis	Calcium homeostasis
Betjes et al. [14]	Requiring transfusion, bleeding at critical site, >2 g/dL ↓ in hemoglobin <24 h	Persistent TMP >280 mmHg; life span limited to 72 h	No	Yes	Yes	Yes
Fealy et al. [15]	No	TMP >300 mmHg, evidence of visible clot obstructing flow	No	No	No	No
Hetzel et al. [16]	Mild (no systemic symptom), moderate (systemic symptoms and/or Hb ↓ >2 g/dL/day) or severe (need for transfusion)	Yes	30-day mortality	Assessed on D3 and consecutively	No	Yes
Kutsogiannis et al. [17]	>20 mmHg ↓ in BP; >20 bpm ↑ in HR; >2 U RBC transfusion; >2 g/dL ↓ in hemoglobin within 24 h	TMP >200 mmHg, resulting in repeated triggering of "high pressure" alarm	No	Yes	No	Yes
Monchi et al. [18]	Bleeding with severe complication, >2 U RBC transfusion	Persistently high TMP (>300 mmHg) prohibiting the continuation of the therapy	No	Yes	No	Yes
Oudemans-van Straaten et al. [19]	≥2 U RBC transfusion or causing a 0.5 mmol/L ↓ in hemoglobin <24 h	Persistently high TMT (>300 mmHg)	Hospital or 3-month mortality	Yes	Yes	No



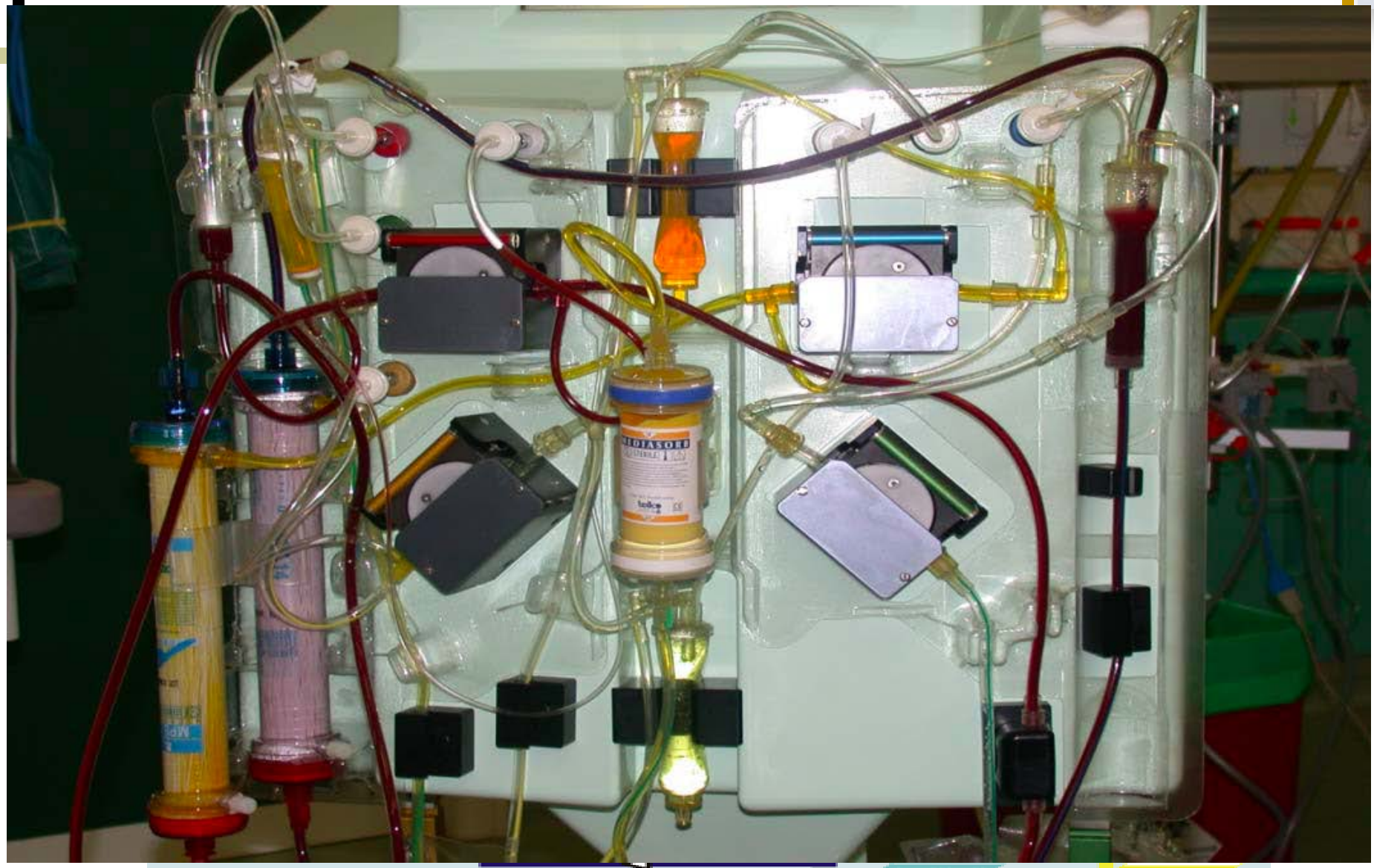
Futur

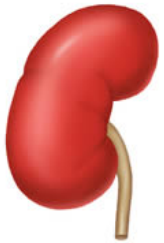


Cascade filtration



CPFA





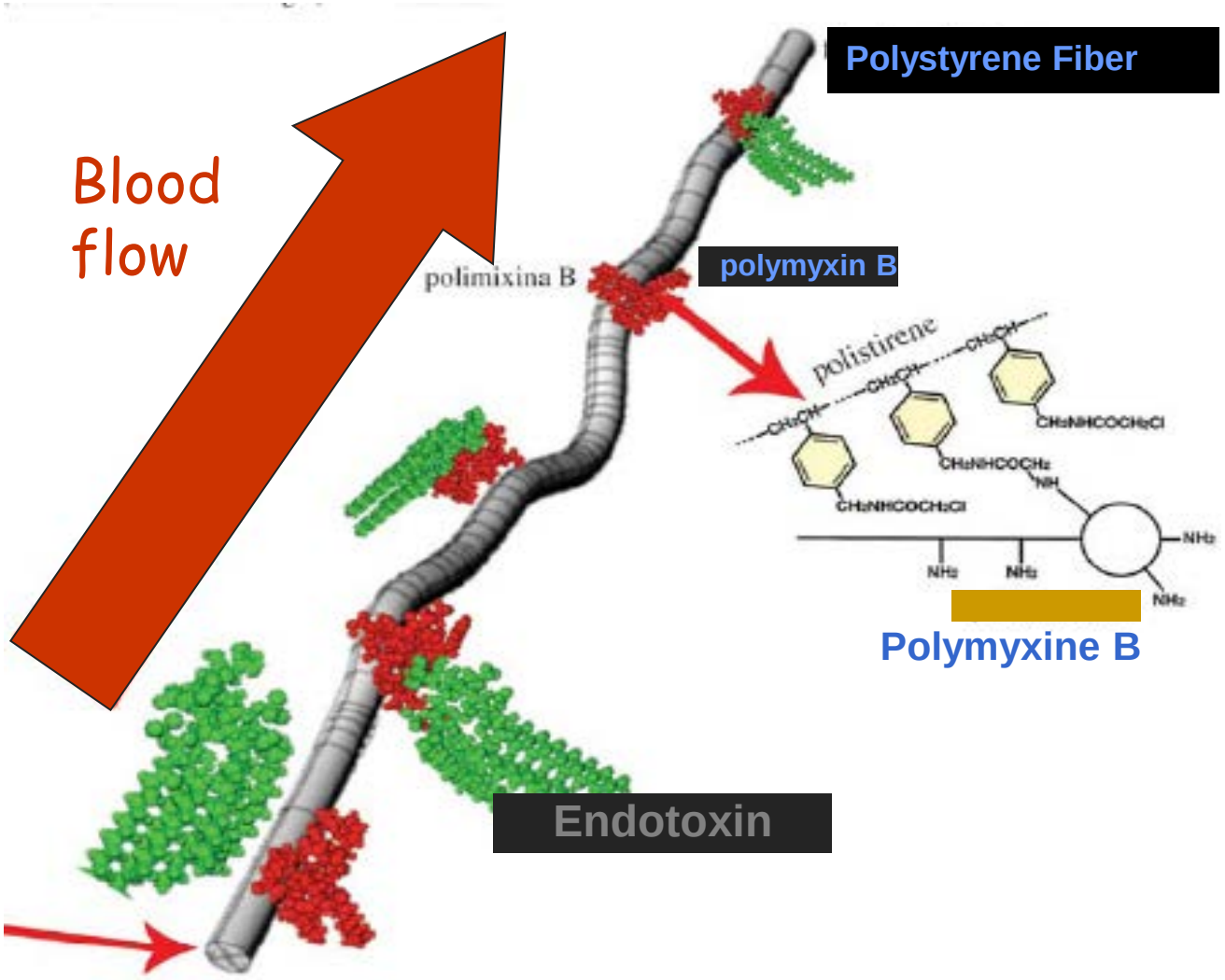
CPFA

- Etude COMPACT (Italie)
- Patients en choc septique
- TTT conventionnel *versus* TTT conventionnel + CPFA
- Mortalité hospitalière
- 330 patients

Début : Décembre 2006

Fin : Juillet 2011

Polymyxin B membrane

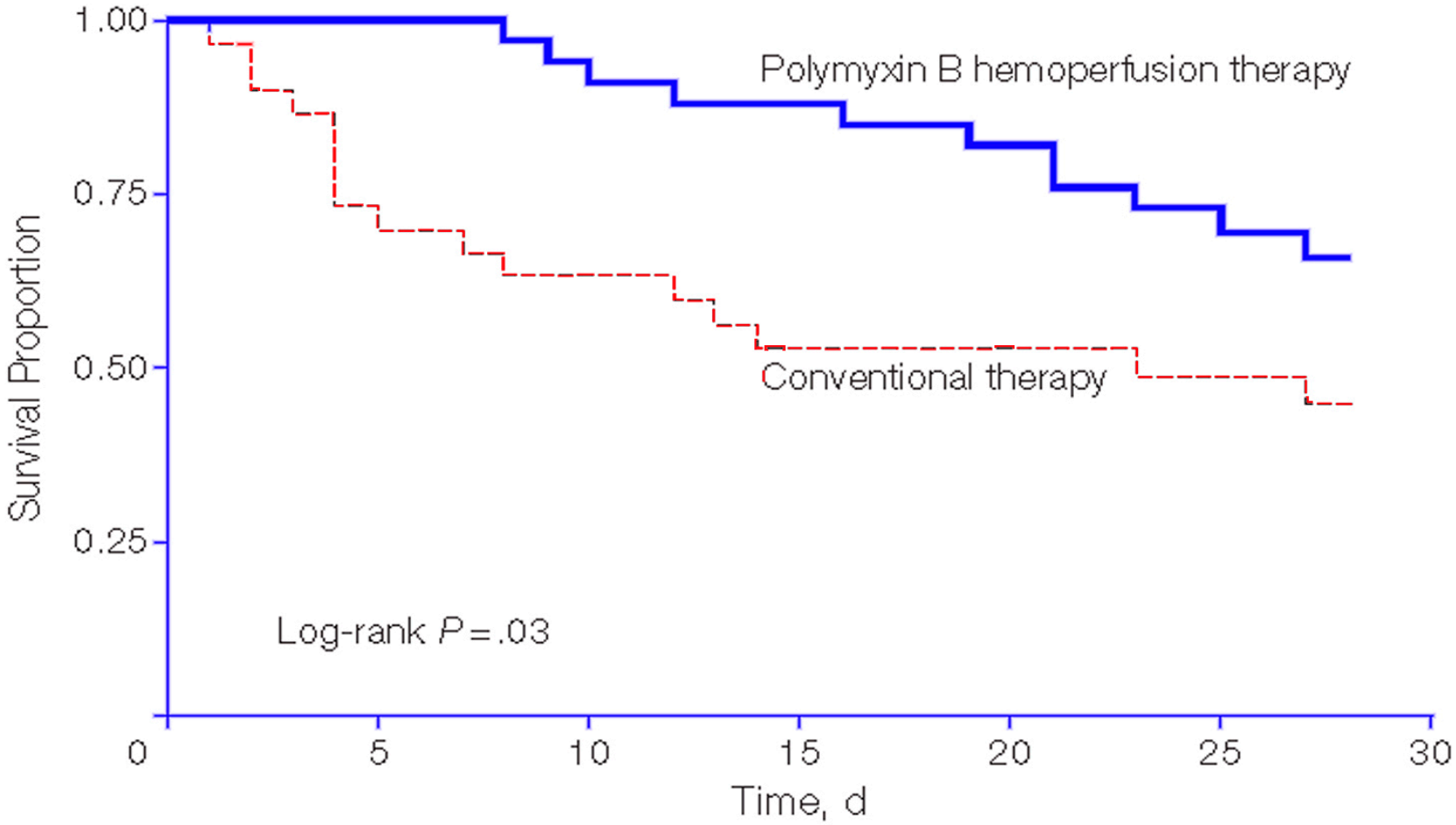


Early Use of Polymyxin B Hemoperfusion in Abdominal Septic Shock

The EUPHAS Randomized Controlled Trial

Dinna N. Cruz, MD, MPH
Massimo Antonelli, MD
Roberto Fumagalli, MD
Francesca Foltran, MD
Nicola Brienza, MD, PhD
Abele Donati, MD
Vincenzo Malcangi, MD
Flavia Petrini, MD
Giada Volta, MD
Franco M. Bobbio Pallavicini, MD
Federica Rottoli, MD
Francesco Giunta, MD
Claudio Ronco, MD

JAMA. 2009;



« ABDO-MIX study »

240 patients avec peritonite et chirurgie

Recours aux vasopresseurs(Noradrenaline) 2 heures après chirurgie

Randomisation Dans les 8 heures post-op

Polymyxin B (X2/24h)

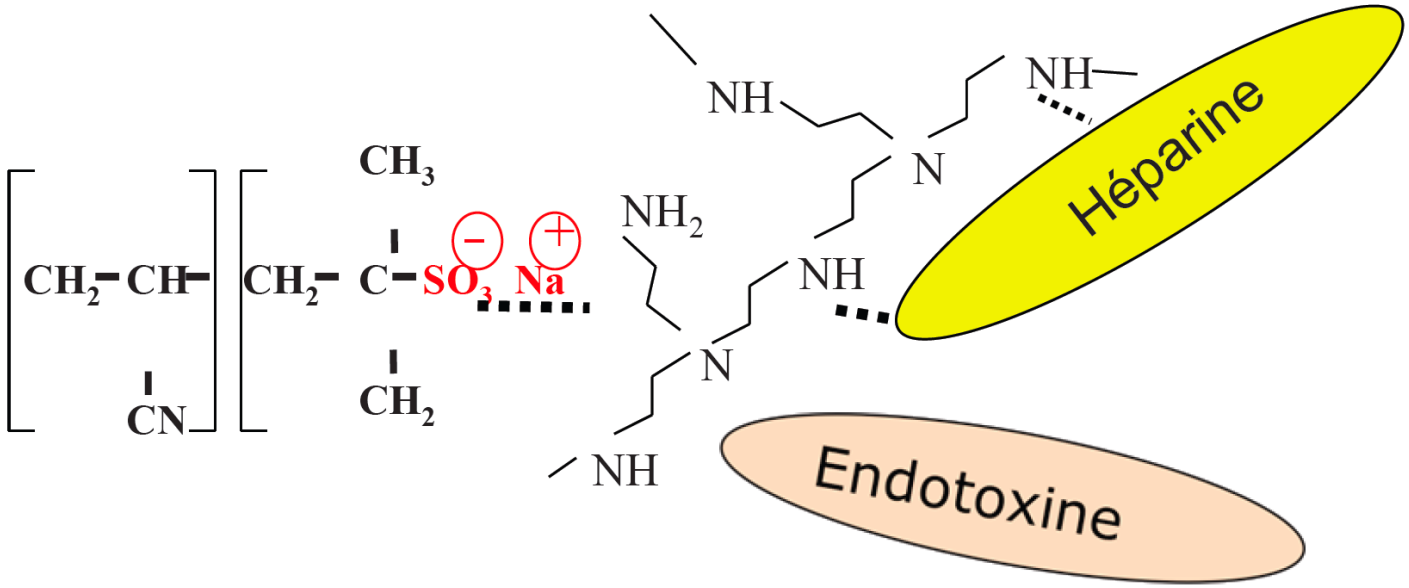
Standard

Mortalité

D28

D90

OXIRIS®



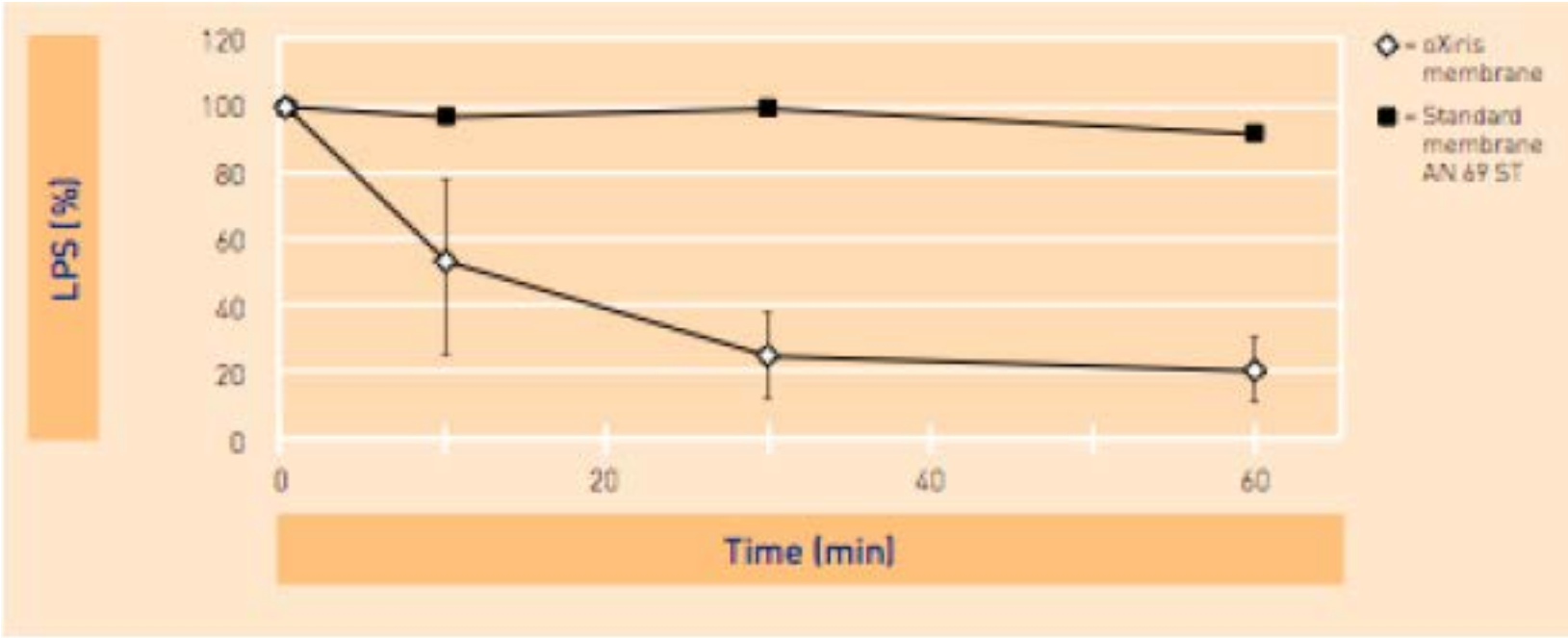
Structure de base (polyacrylonitrile)

AN69

Polycation : Polyethyleneimine

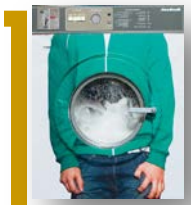
Adsorption des endotoxines (chargées négativement)

OXIRIS®



Données in vitro

High-volume haemofiltration with a new haemofiltration membrane having enhanced adsorption properties in septic pigs



Thomas Rimmelé[1,2,3], Abdulnasser Assadi[2], Mathilde Cattenoz[1], Olivier Desebbe[2,3], Corine Lambert[4], Emmanuel Boselli[1,3], Joëlle Goudable[3,5], Jérôme Étienne[3,6], Dominique Chassard[1,3], Giampiero Bricca[2,3] and Bernard Allaouchiche[1,2,3]

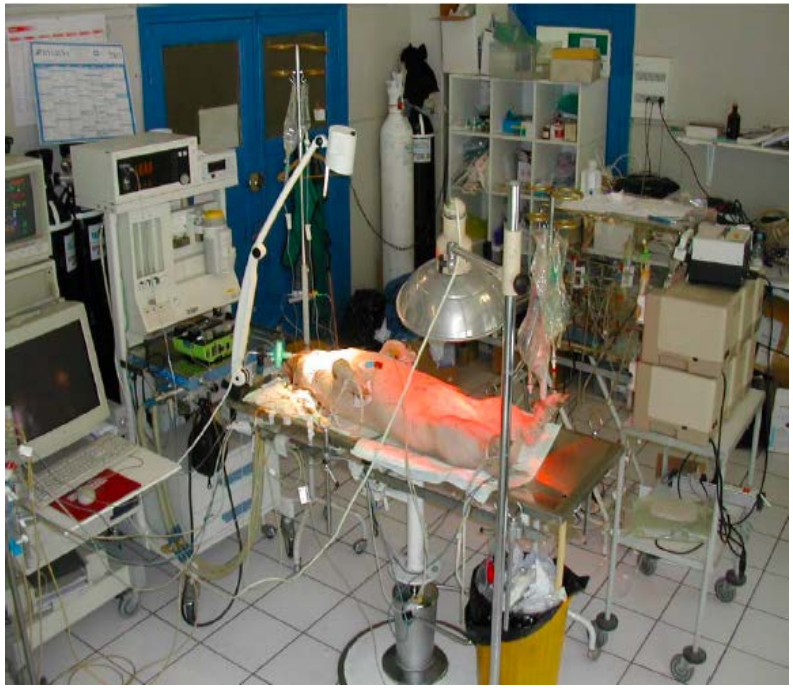
Nephrol Dial Transplant (2009)

Table 3. Mean ± SD haemodynamic and biochemical parameters after a 6-h HVHF session, at T6

	AN69 mb ($n = 10$)	Treated mb ($n = 10$)	P-value
HR (beats/min)	138 ± 20	148 ± 16	0.23
MAP (mmHg)	64 ± 6	59 ± 8	0.13
SPAP (mmHg)	39 ± 9	30 ± 8	0.029
MPAP (mmHg)	34 ± 8	24 ± 7	0.008
PCWP (mmHg)	12 ± 3	11 ± 4	0.53
CO (l/min)	6.9 ± 4.8	5.5 ± 2.8	0.44
SAR (dyn/s/cm^5)	672 ± 205	797 ± 346	0.34
PAR (dyn/s/cm^5)	325 ± 186	234 ± 148	0.24
Epinephrine (mg)	3.27 ± 3.02	2.11 ± 1.05	0.27
Crystalloids (ml)	7587 ± 1456	5937 ± 1588	0.026
Hydroxyethylstarch (ml)	1912 ± 538	1437 ± 320	0.027
pH	7.10 ± 0.07	7.20 ± 0.11	0.026
Lactate (mmol/l)	14.11 ± 3.36	9.61 ± 4.47	0.02

Table 4. Mean ± SD serum endotoxins levels (EU/ml)

	AN69 mb ($n = 10$)	Treated mb ($n = 10$)
T0	3.98 ± 3.31	4.26 ± 7.68
T1	11.07 ± 10.64	1.91 ± 1.19[a]
T6	2.96 ± 2.75	2.26 ± 2.39



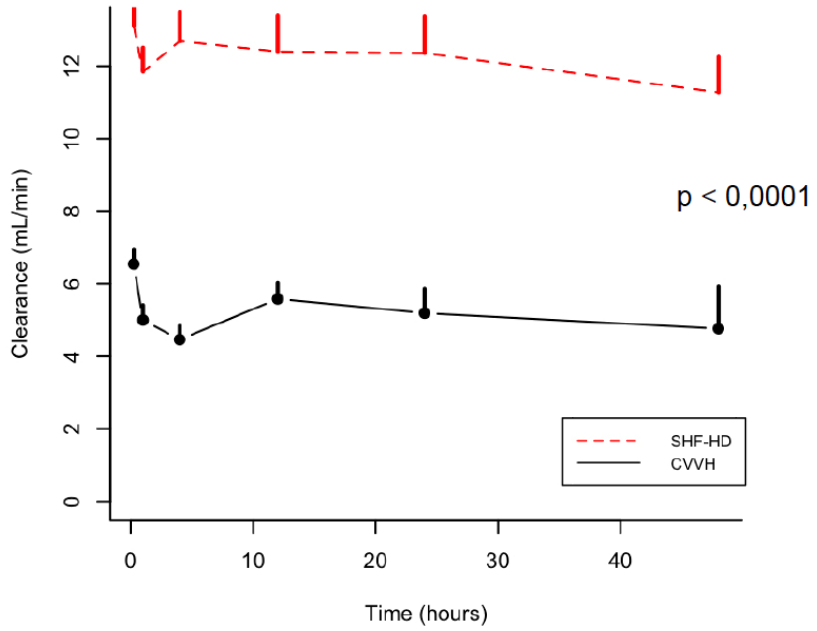
D'après T. Rimmelé

SEPTEX® et EMIC2®

Augmentation de la clairance des moyennes molécules en comparaison à l'EER standard (HCO-HF et HCO-HD)

Morgera et al. NDT2003
Haase et al. AJKD 2007

Chaines Kappa des Ig



Capture de leucocytes activés

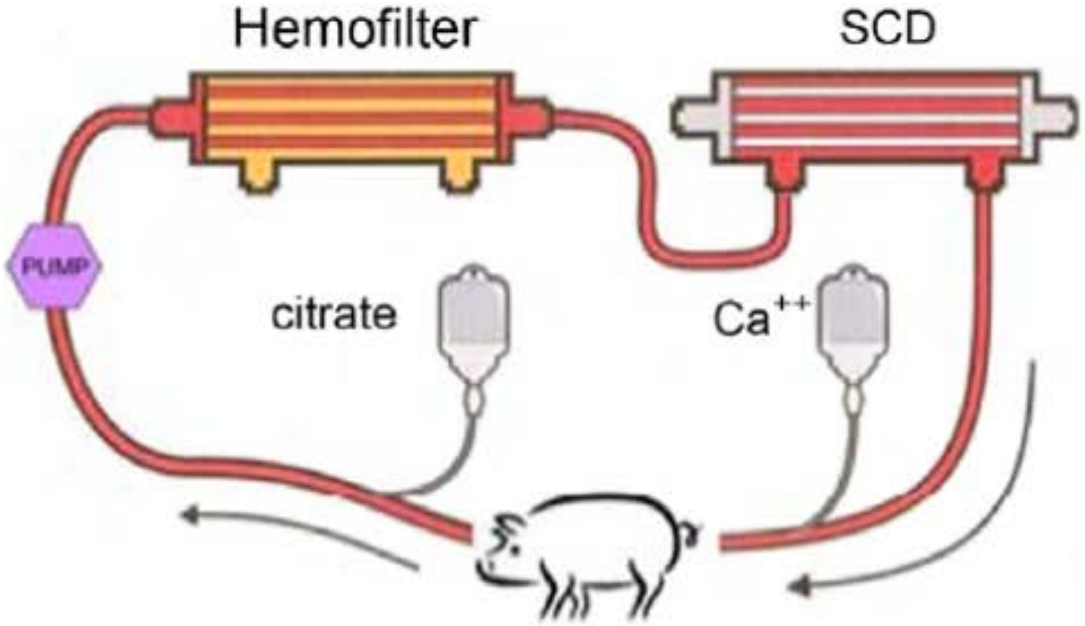
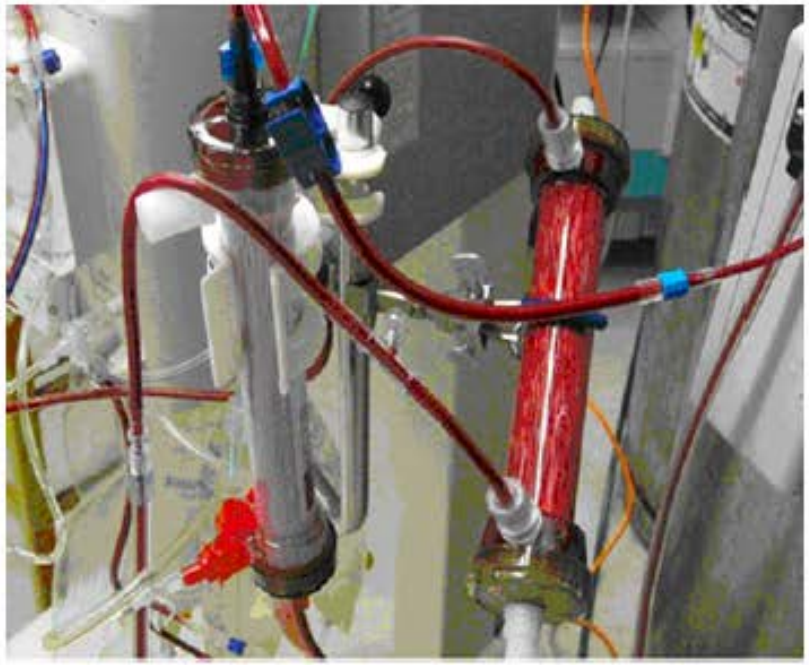
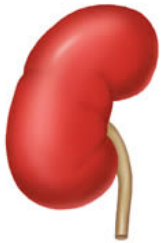


Figure 1. Extracorporeal circuit with SCD.
doi:10.1371/journal.pone.0018584.g001



Ding F et al. PLoS One.

D'après T. Rimmelé



Le coté obscur

The "Depletion syndrome"

- Albumin (Carriers)
- Catecholamines
- Drugs Antibiotics
- Microconutrients
  - Trace Elements
  - Hydrosolubles Vitamines
  - Amino-Acids
- Energy
- Macronutrients

Frankenfield et al. Nutrition 1995;11:388-393

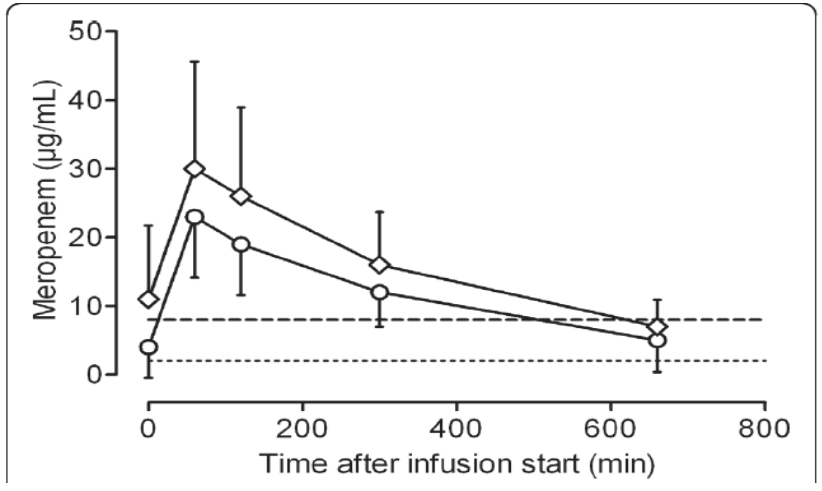
Recommended β-lactam regimens are inadequate in septic patients treated with continuous renal replacement therapy

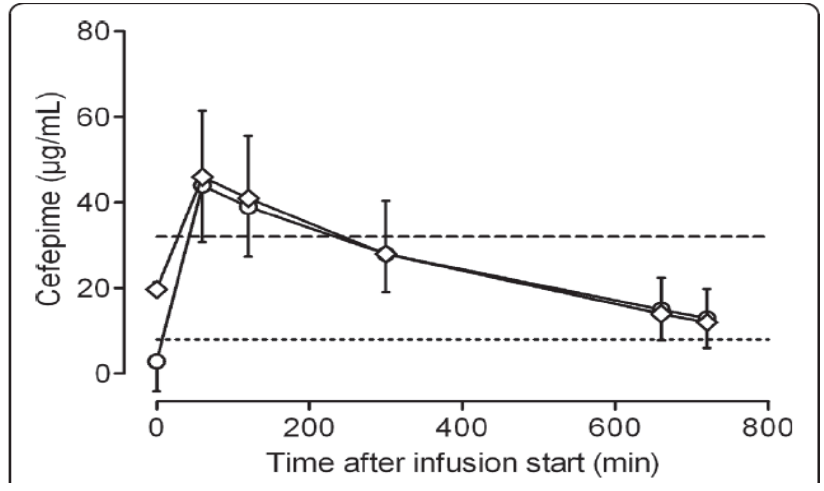
Critical Care 2011

Lucie Seyler[1], Frédéric Cotton[2], Fabio Silvio Taccone[3], Daniel De Backer[3], Pascale Macours[2], Jean-Louis Vincent[3] and Frédérique Jacobs[1*]

Table 2 Pharmacokinetic parameters of the four antibiotics

Antibiotic (number of series)	V_d (l/kg)	C_{max} (μg/ml)	C_{min} (μg/ml)	AUC (mg/hour/ml)	CL (ml/minute/kg)	$t_{1/2}$ (hours)
MEM 1 g twice daily (n = 22)	0.45 (0.20 to 3.03)	26 (15 to 67)	6 (2 to 11)	134 (61 to 291)	1.15 (0.54 to 3.37)	4.39 (2.61 to 30.5)
TZP 4.0/0.5 g four times daily (n = 21)	0.44 (0.22 to 1.72)	138 (36 to 262)	60 (4 to 155)	527 (62 to 1378)	1.15 (0.27 to 6.26)	4.16 (1.05 to 15.3)
FEP 2 g twice daily (n = 11)	0.55 (0.33 to 0.94)	43 (28 to 83)	11 (3 to 22)	379 (148 to 483)	1.04 (0.43 to 2.97)	6.17 (3.30 to 22.9)
CAZ 2 g twice daily (n = 15)	0.37 (0.22 to 0.84)	78 (54 to 118)	24 (5 to 46)	536 (258 to 906)	0.52 (0.13 to 1.61)	7.74 (2.52 to 33.5)





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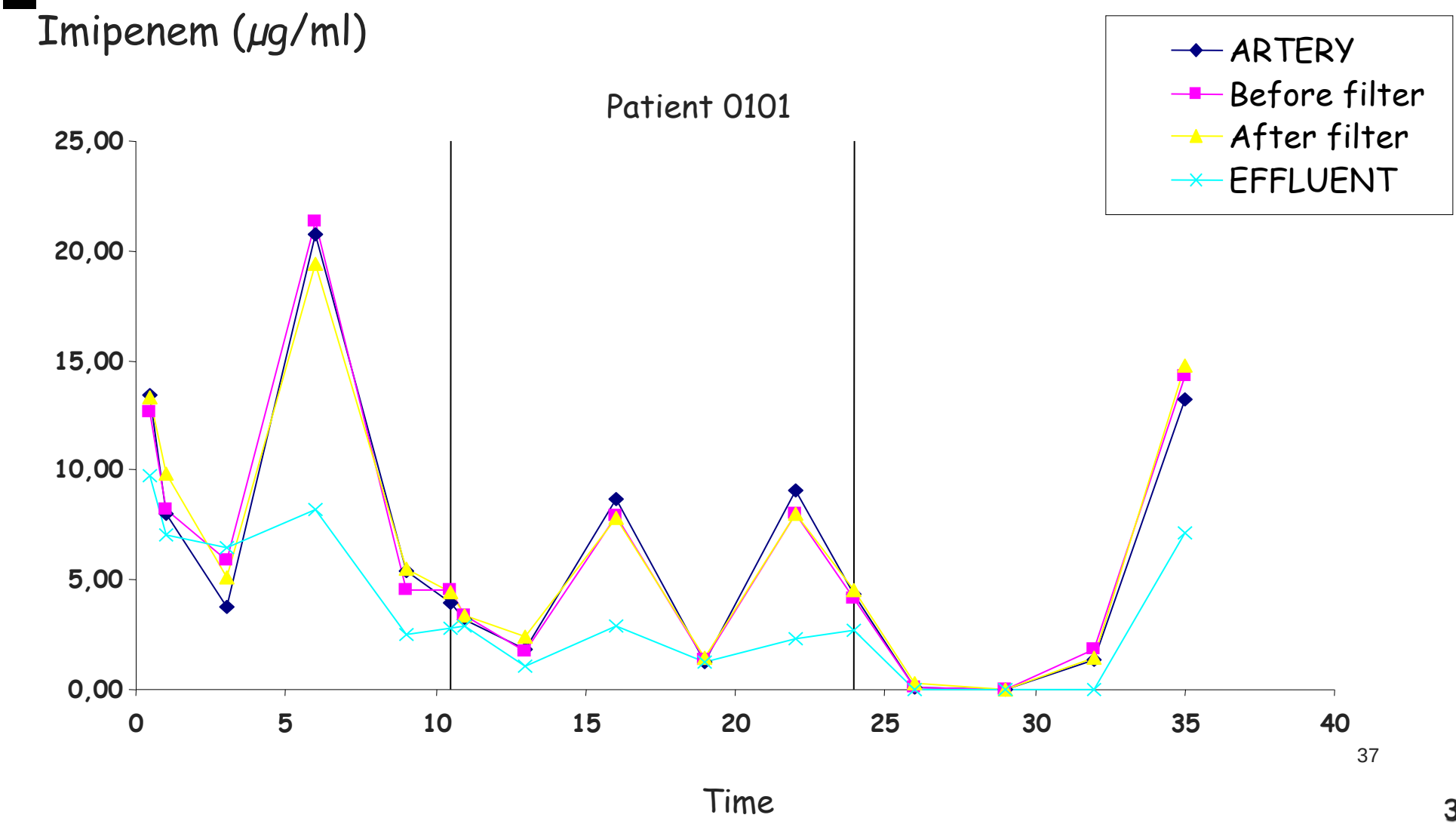

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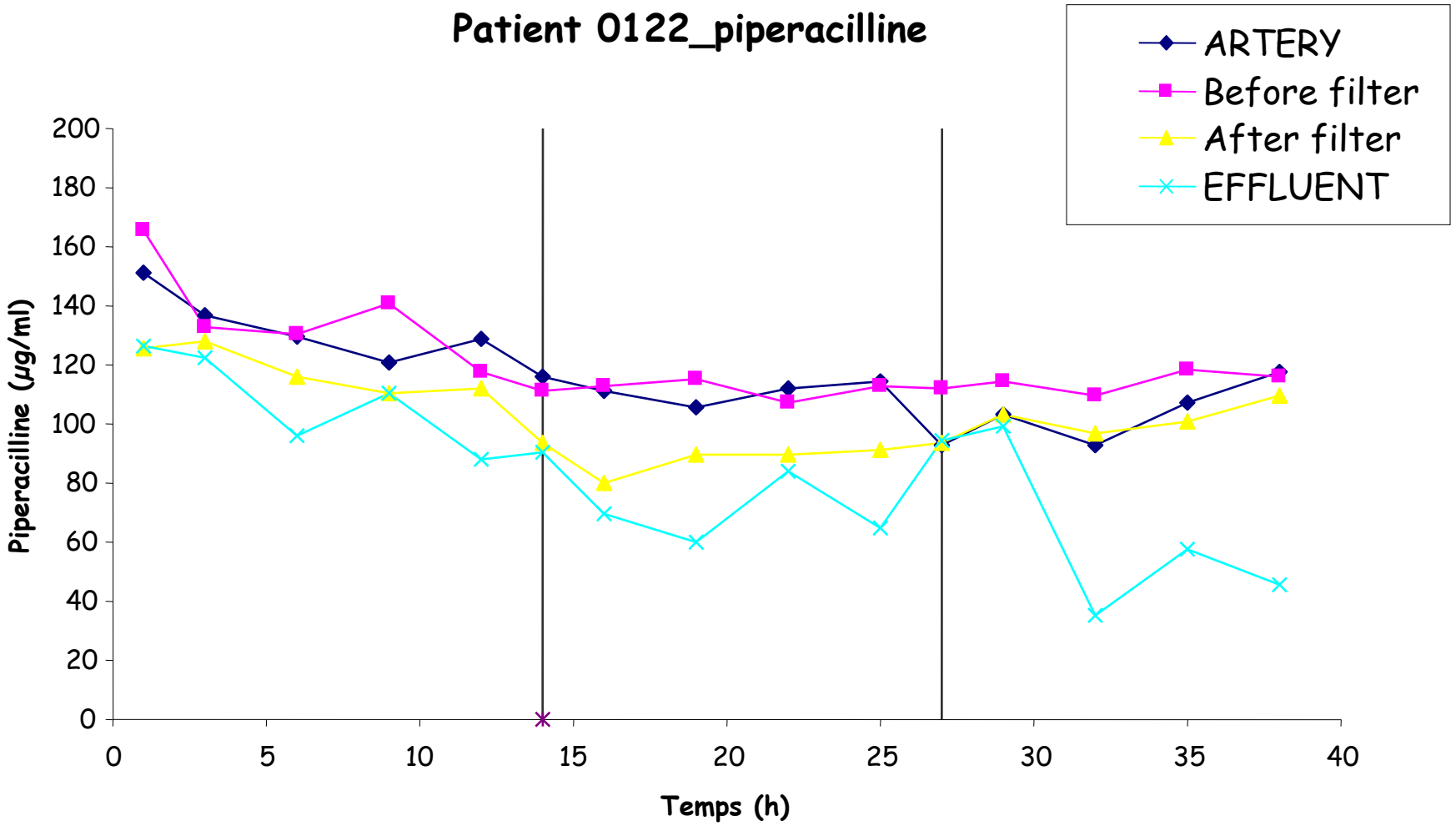

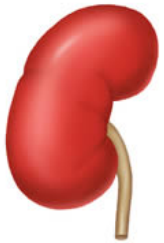

Conclusion

- ✓ HDI = CVVH mais préférer le continue à la phase aigüe et patients instables
- ✓ Pas de haut volume dans le sepsis
- ✓ Démarrer rapidement mais pas avant AKI
- ✓ Privilégier le citrate mais…FORMATION
- ✓ Evaluer les membranes adsorbantes
- ✓ Ne pas oublier le côté obscur…

Conclusion