ANTE 2022 Dialisi e Tecnologia

“La Scelta della Membrana Dialitica”

Moderatori: P. Fabbrini, E.Fiaccadori

Membrane a Medio ed Alto Cut-Off: quando le uso?

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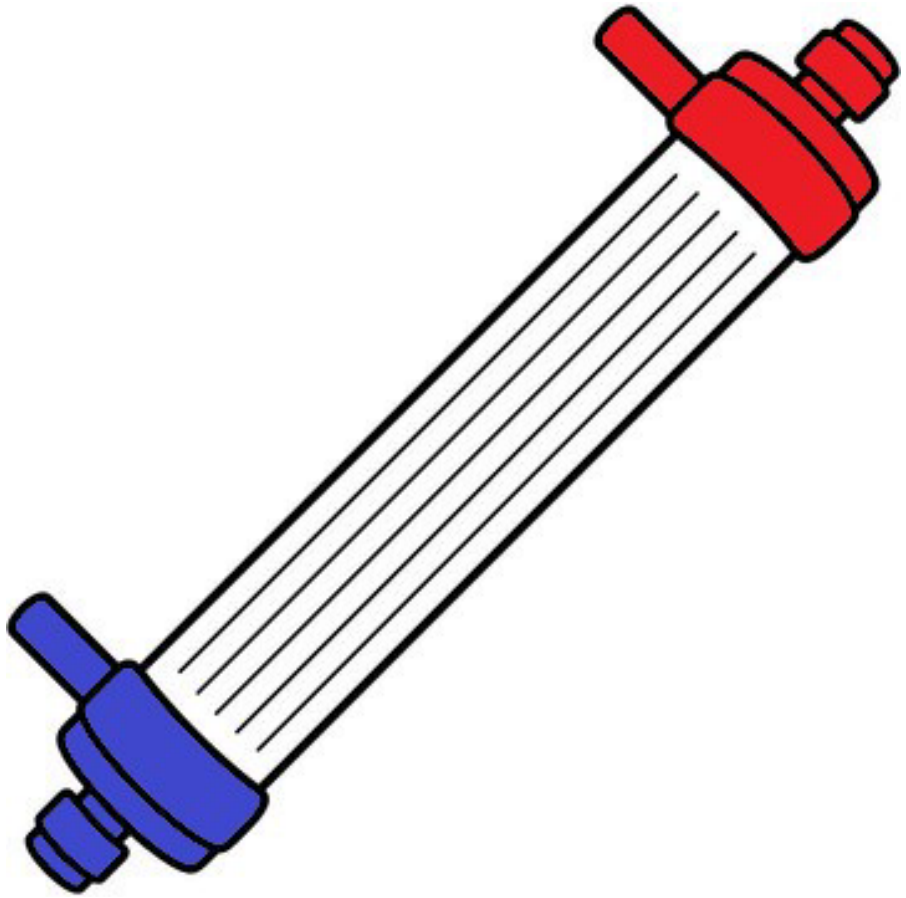
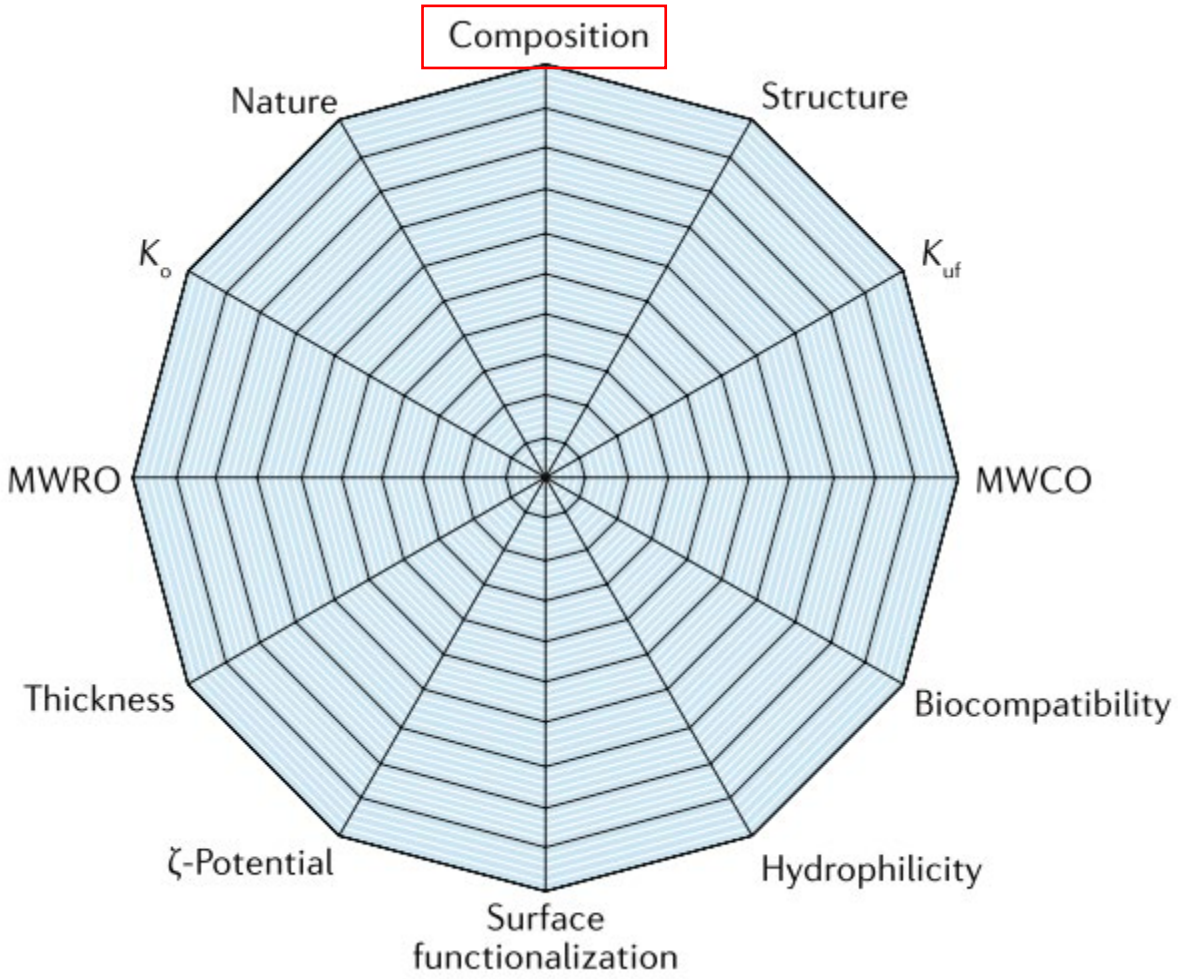
Policlinico

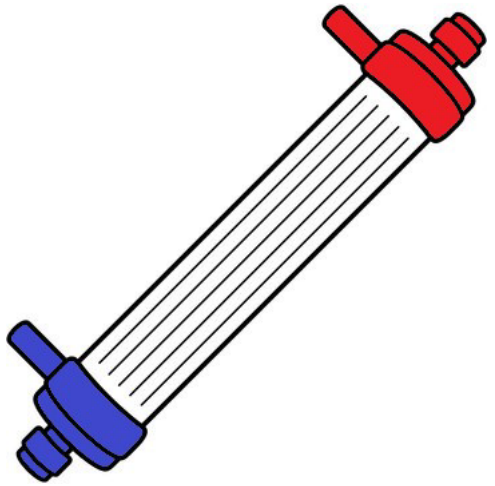


Tradizionalmente si classificavano le membrane per la loro composizione

- Cellulosiche
- Sintetiche

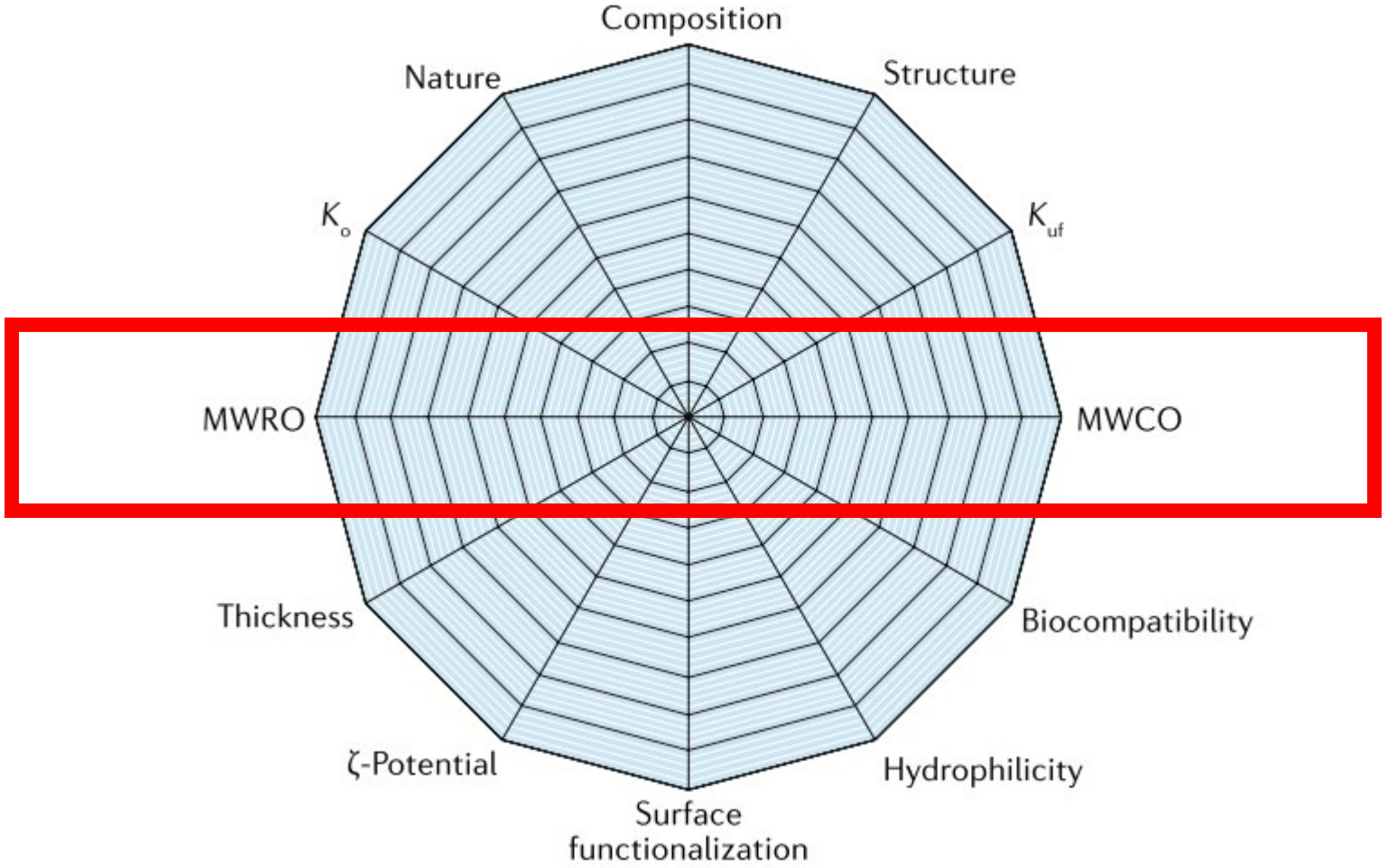
Ronco C. Clark WR. Hemodialysis Membranes
Nat Rev Nephrol 2018





Grazie all'evoluzione tecnica nella produzione di filtri da dialisi, **nuovi parametri** sono entrati in gioco.

Ronco C. Clark WR. Hemodialysis Membranes *Nat Rev Nephrol* 2018



Ronco C. Clark WR. Hemodialysis Membranes
Nat Rev Nephrol 2018

Cosa intendono queste sigle?

1

SC – Coefficiente di Sieving (SC)

- Rapporto tra la concentrazione di un soluto X nel filtrato e la concentrazione nel sangue
- Valore compreso fra 0 (nessuna rimozione) e 1 (rimozione completa)

2

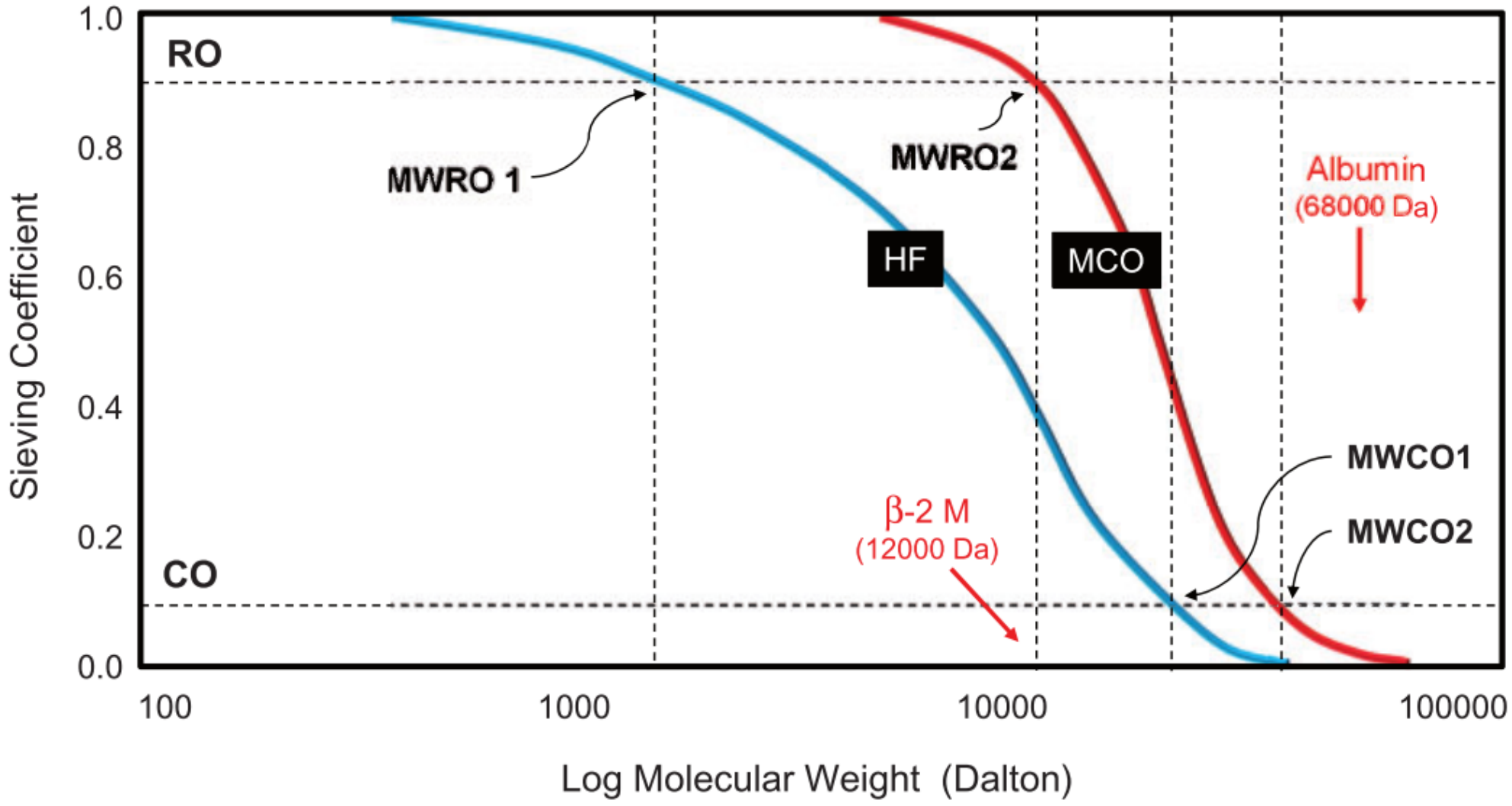
MWCO – Molecular Weight Cut-off

→ Valore di peso molecolare per cui il 10% di X è rimosso dalla membrana (SC 0,1)

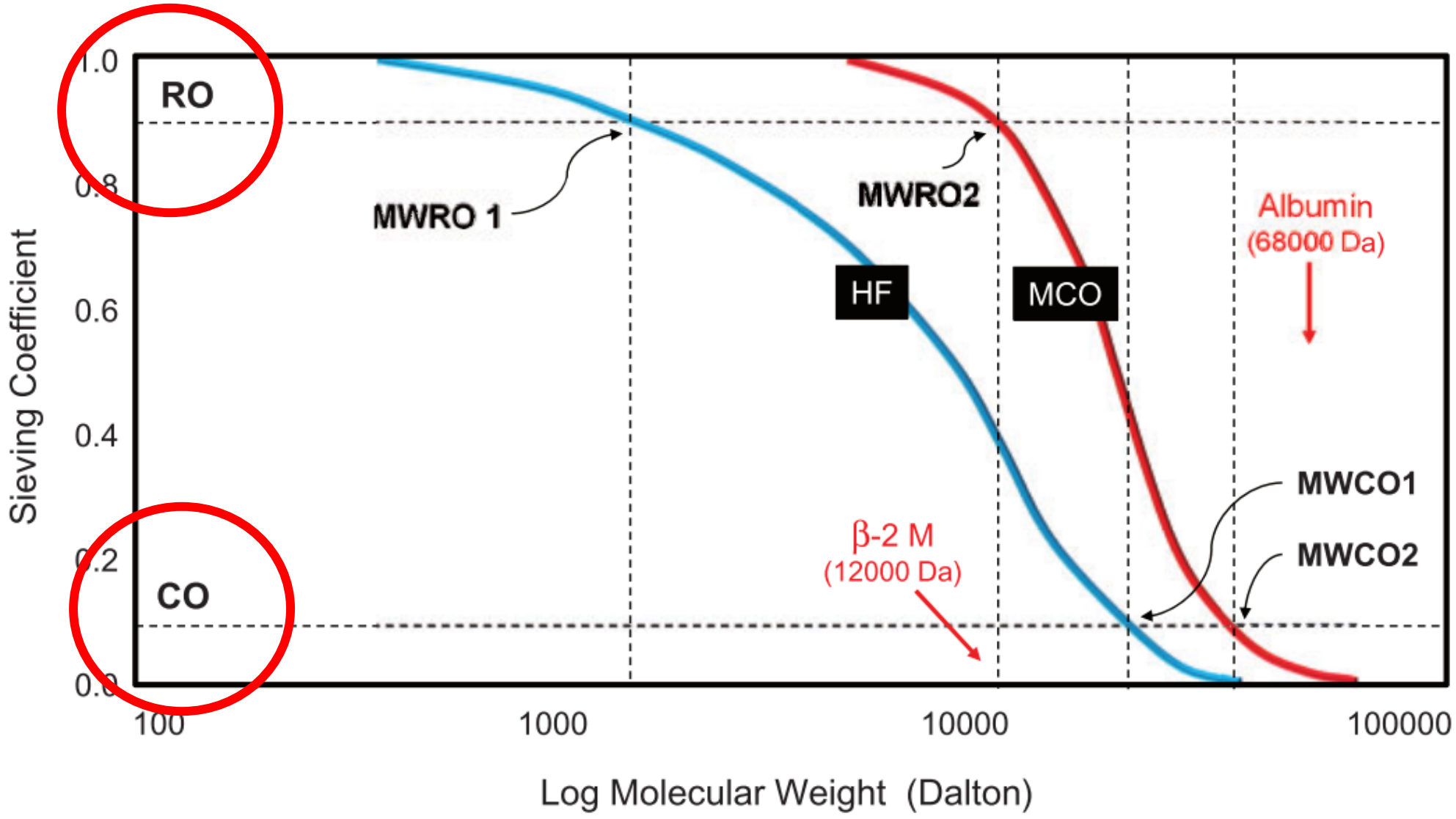
3

MWRO – Molecular Weight Retention Onset

→ Valore di peso molecolare per cui il 10% di X è trattenuto dalla membrana (SC 0,9)



Ronco C. et al. Expanded haemodialysis: from operational mechanism to clinical results *Nephrol Dial Transplant (2018)*



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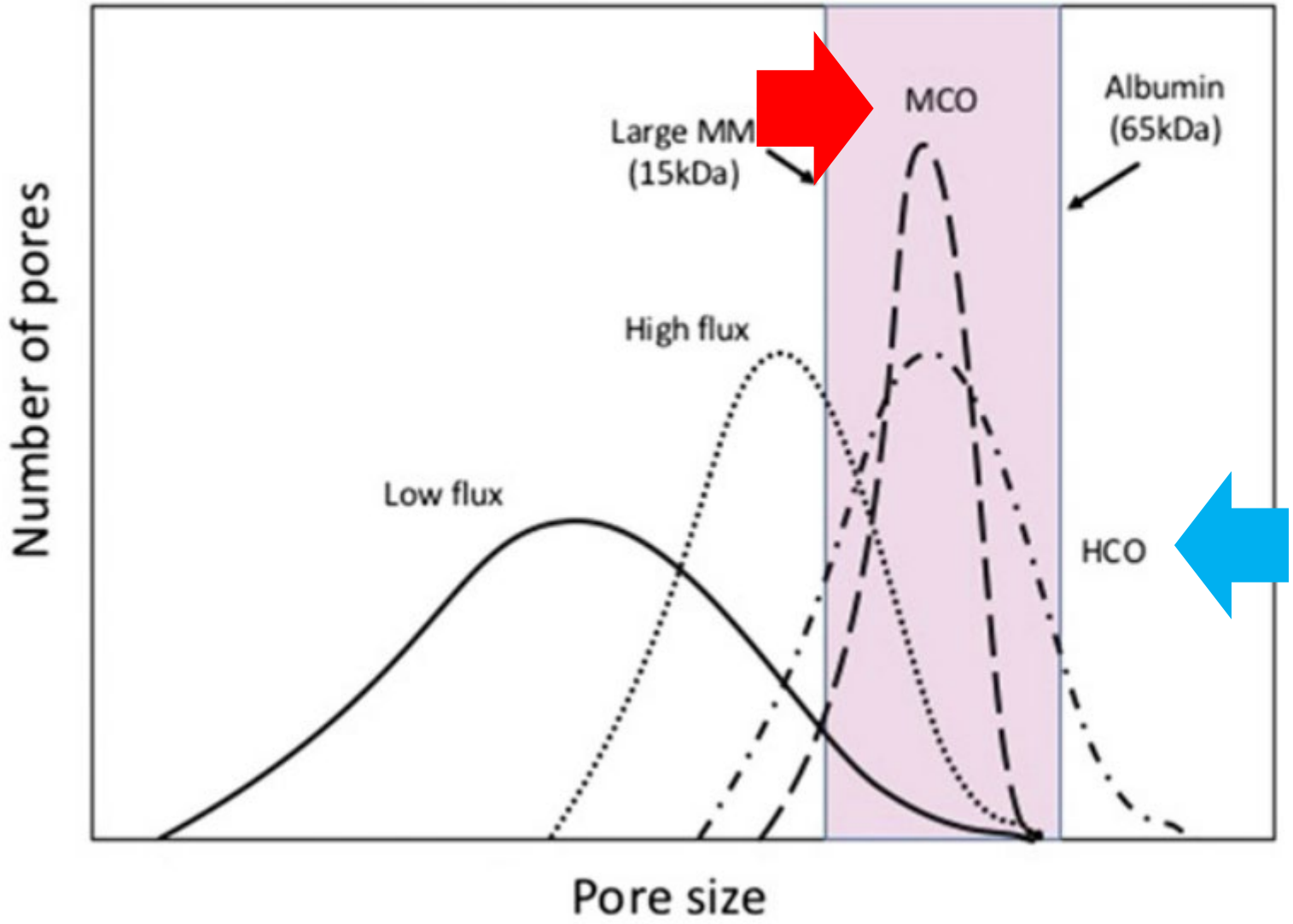
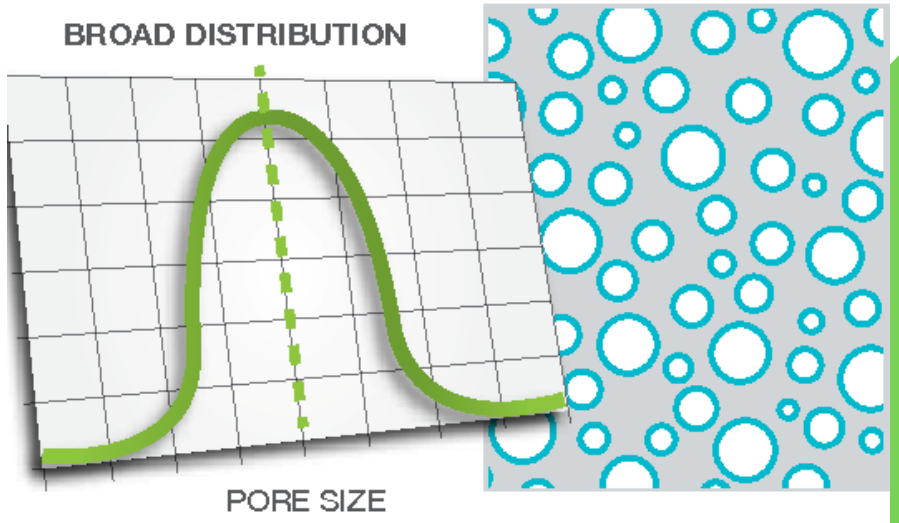
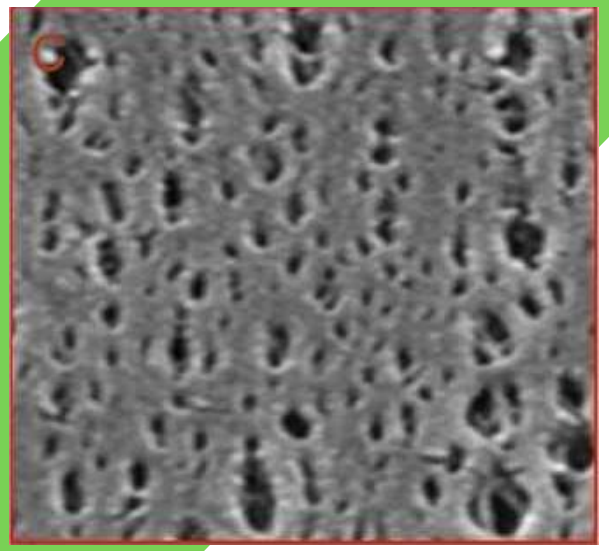


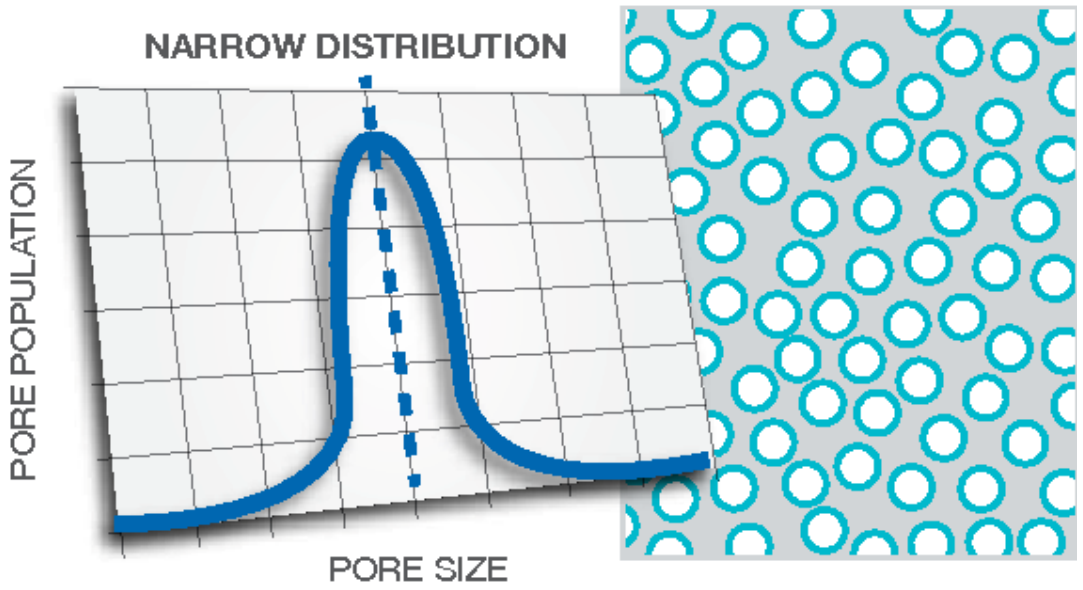
Wolley M. et al Exploring the Clinical Relevance of Providing Increased Removal of Large Middle Molecules *CJASN 2018*

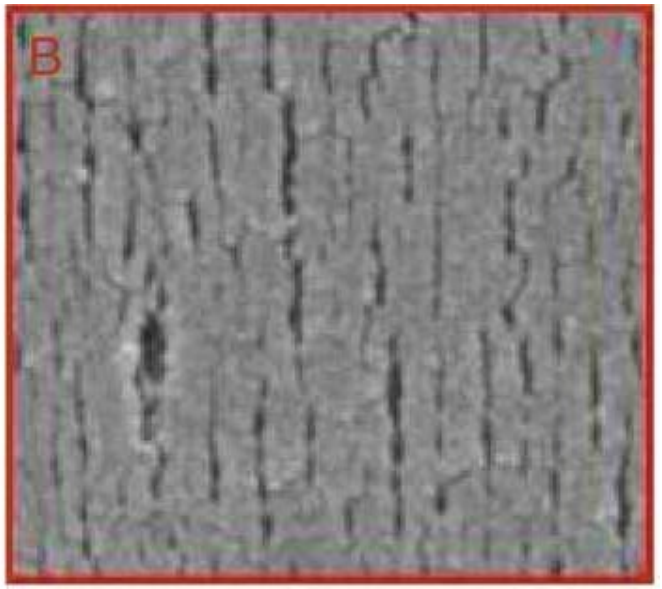




A cosa è dovuta questa differenza?

A Clinical Update on Dialyzer Membranes State-of-the-Art Considerations for Optimal Care in Hemodialysis. – NKF 2013





Blood Purification

Editorial

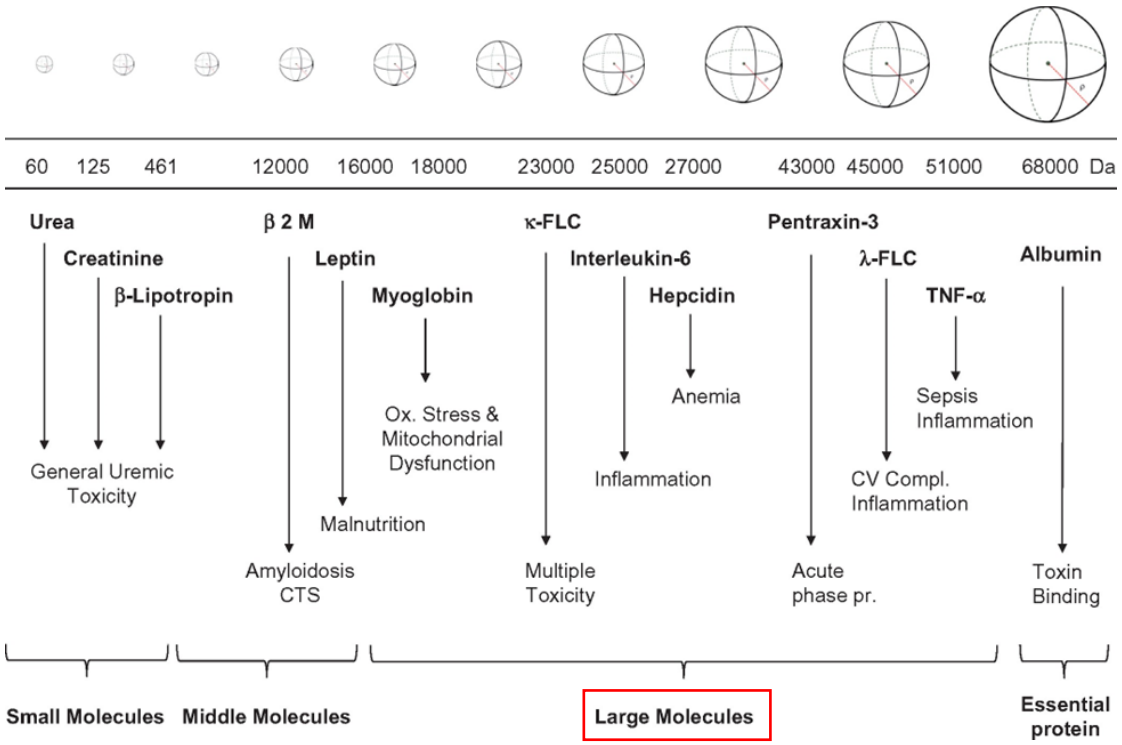
Blood Purif 2017;44:I–VIII
DOI: 10.1159/000476012

Published online: May 10, 2017

The Rise of Expanded Hemodialysis

Claudio Ronco[a, b]

[a]Department of Nephrology Dialysis and Transplantation, St. Bortolo Hospital, and [b]International Renal Research Institute, Vicenza, Italy

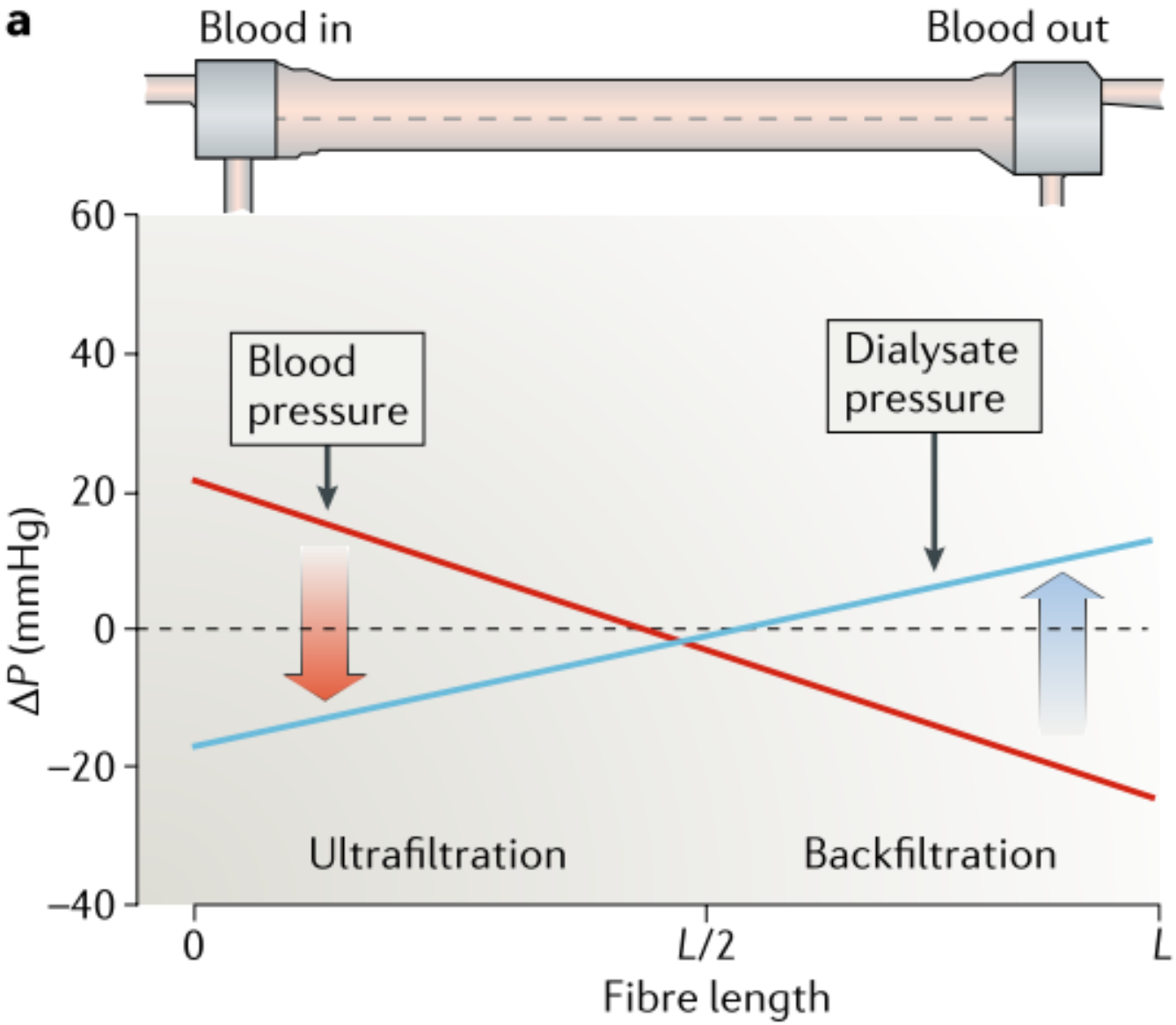


Membrane a Medio e ad Alto Cut Off: Caratteristiche

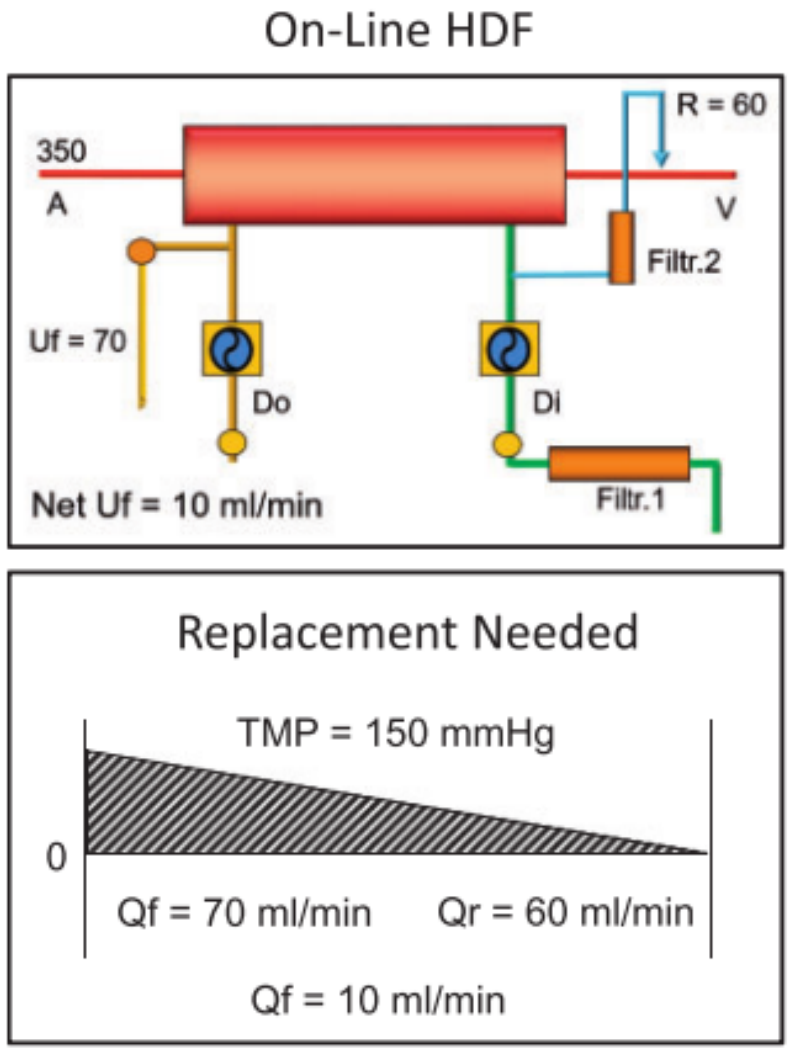
Membrana	MWRO (kDa)	MWCO (kDa)	Raggio dei pori (nm)
Alto flusso	4,4 ± 0,3	14,2 ± 0,2	2,7 ± 0,0
Medio Cut off	6,8 ± 0,1	25 ± 5	3,5 ± 0,3
Alto Cut off	8,1 ± 0,8	40 ± 8	4,3 ± 0,4

Boschetti de Fierro A. et al. MCO membranes: enhanced selectivity in high flux class. *Scient Rep (2015)*

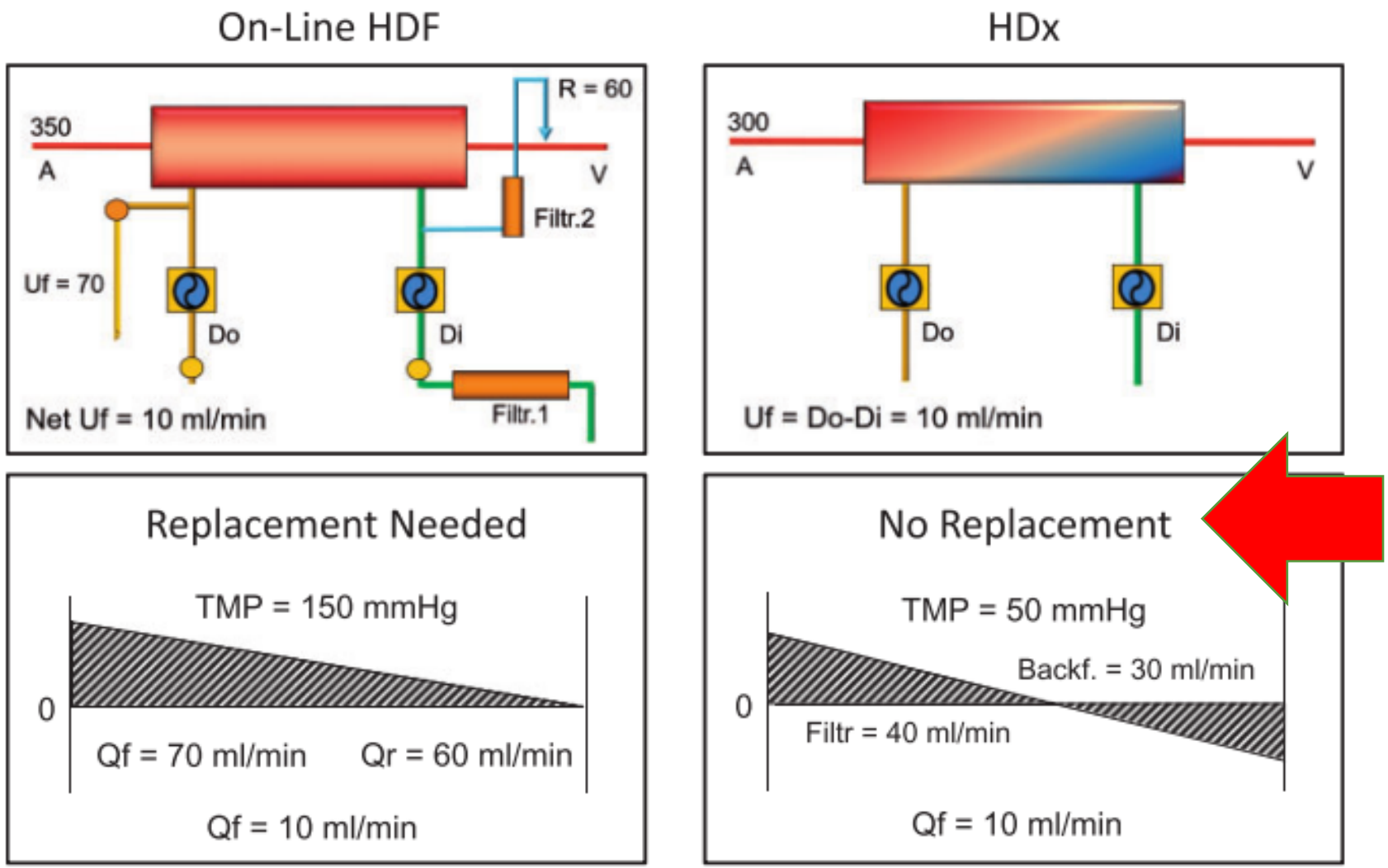
Non solo diffusione, ma anche convezione:



Ronco C. &v Clark WR. Hemodialysis Membranes *Nat Rev Nephrol* 2018



Ronco C. et al. Expanded haemodialysis: from operational mechanism to clinical results *Nephrol Dial Transplant (2018)*

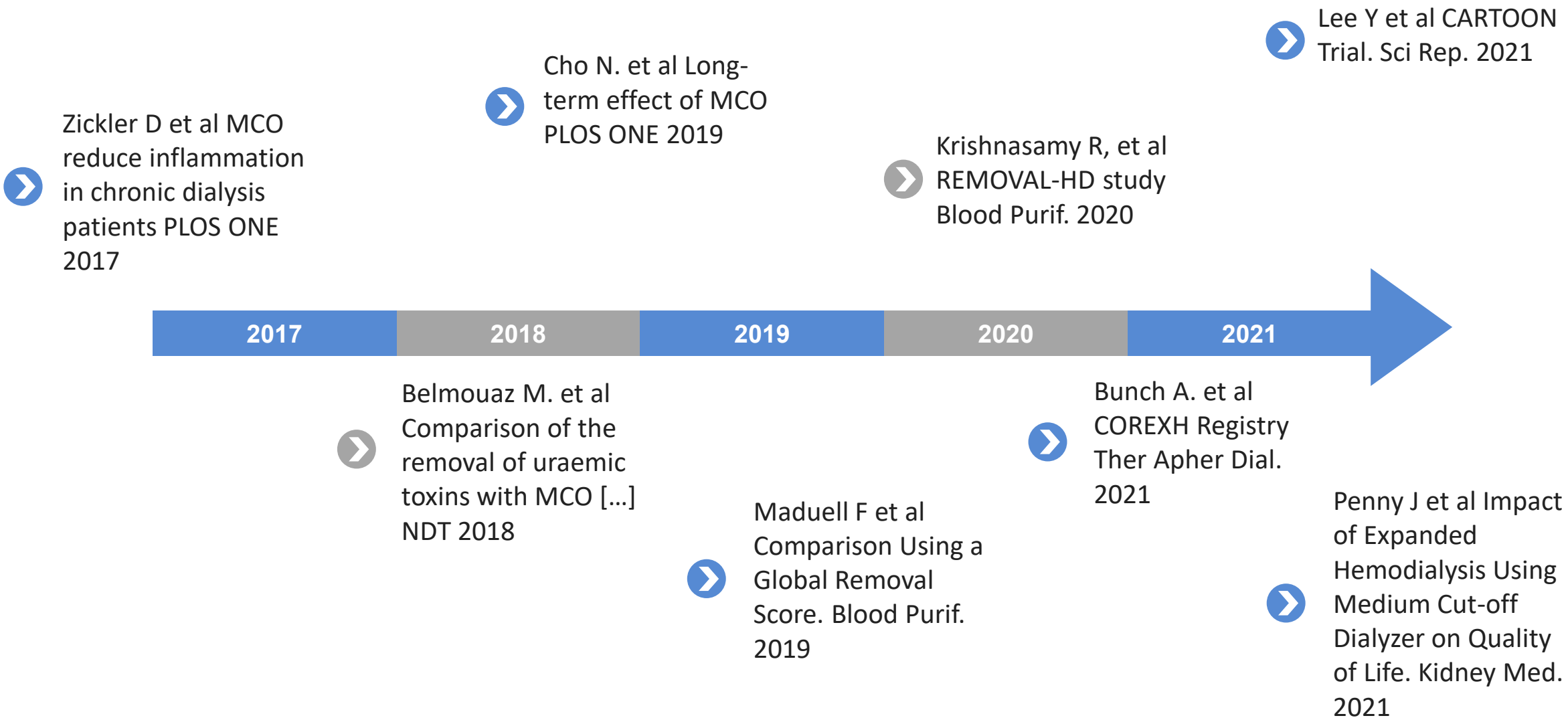


Ronco C. et al. Expanded haemodialysis: from operational mechanism to clinical results *Nephrol Dial Transplant (2018)*

Dalla Teoria…

…alla Pratica.

Impiego delle Membrane a Medio Cut-Off



1

INDICAZIONI

MEDIO CUT-OFF

1. **Alternativa all' Emodiafiltrazione On-Line**
   - **Non applicabilità clinica OL- HDF**
   - **Non applicabilità tecnica OL- HDF**
2. **Riduzione delle Calcificazioni vascolari**

Artificial
Organs

Dialysis and Patient Factors Which Determine Convective Volume Exchange in Patients Treated by Postdilution Online Hemodiafiltration

TABLE 4. *Multivariable step backward linear model for substitution volume achieved with online postdilutional hemodiafiltration corrected for dialysis session time and body surface area*

Variable	β	SE	St β	t	95% CI	P
Dialysate flow rate	0.07	0.001	0.34	9.5	0.05–0.08	<0.001
Pre ECW	−0.70	0.096	−0.3	−7.3	−0.9 to −0.51	<0.001
Blood flow rate	0.05	0.011	0.18	4.7	0.03–0.08	<0.001
Tinzaparin dose	−0.001	0.00	−0.14	−3.8	−0.002 to −0.001	<0.001
Dialyzer surface area	−5.2	1.48	−0.14	−3.5	−8.1 to −2.3	<0.001
Diabetic	−1.61	0.6	−0.96	−2.7	−2.8 to −0.42	0.008
Log dialysis vintage	1.5	0.65	0.08	2.3	0.23–2.77	0.021
Log CRP	−1.23	0.57	−0.08	−2.2	−2.4 to −0.11	0.032

“Patients with greater comorbidity were less likely to achieve the higher convective volume exchanges currently reported to be associated with improved survival”

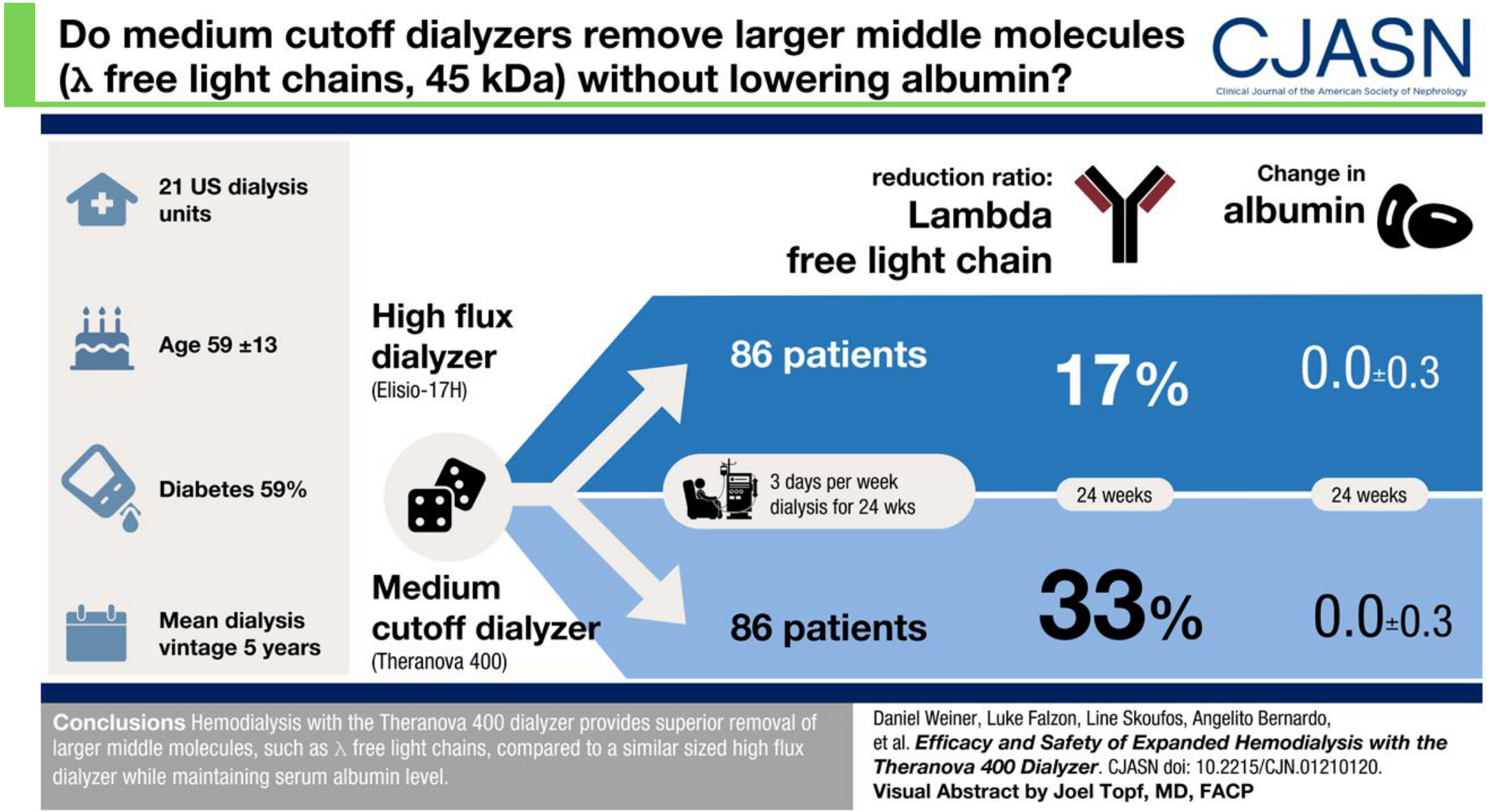
Davenport A. Artif Organs 2016; 40(12):1121-1127

Raccomandazioni per ottenere la Dose di Volume Convettivo Ottimale in HDF on-line

	Prescrizione	Raccomandazioni
Accesso Vascolare	Fistola o Protesi CVC	Prima scelta Aumentare tempo dialisi
Flusso ematico (Qb)	300-500 ml/min	Il massimo possibile
Flusso dialisato	400-500 ml/min + flusso infusato	Non influenza dose dialitica
Flusso infusato	25-33% del Qb = 90-160 ml/min	Il massimo possibile
Durata	4-5 ore /seduta	Il massimo possibile
Volume Convettivo (volume di sostituzione + calo peso)	>23 litri /seduta	Il massimo possibile
Percentuale del Volume Convettivo rispetto al flusso sangue	25-30%	Il massimo possibile
Filtro dializzatore	Membrana ad alto flusso Kuf > 40 ml/h/mmHg	Evitare membrane con alta capacità adsorbitiva

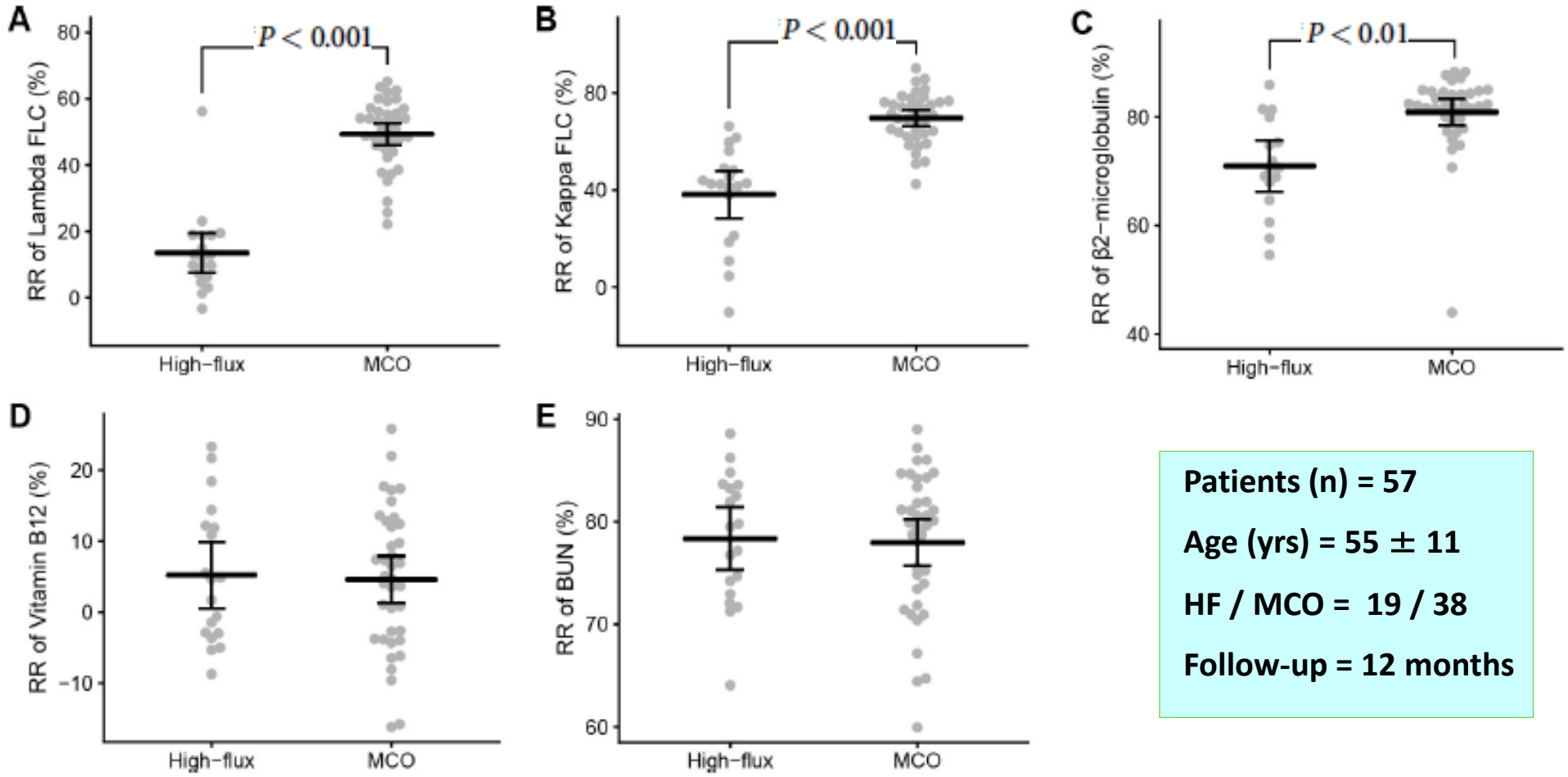
Maduell F. Blood Purif 2015; 40 suppl 1: 17-23

Alternativa a OL-HDF: Efficacia



Alternativa a OL-HDF: Efficacia

Uremic Toxins– High Flux Hemodialysis vs Medium Cut-off Dialysis (observational study)



Patients (n) = 57

Age (yrs) = 55 ± 11

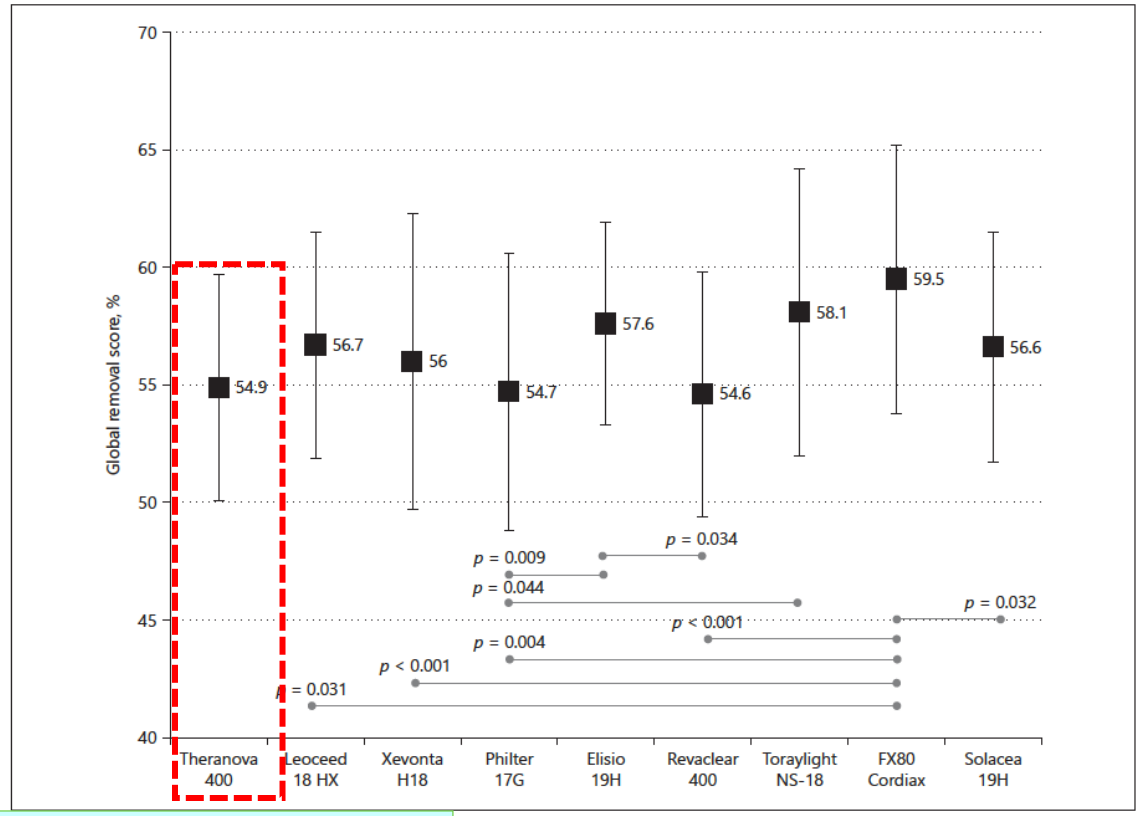
HF / MCO = 19 / 38

Follow-up = 12 months

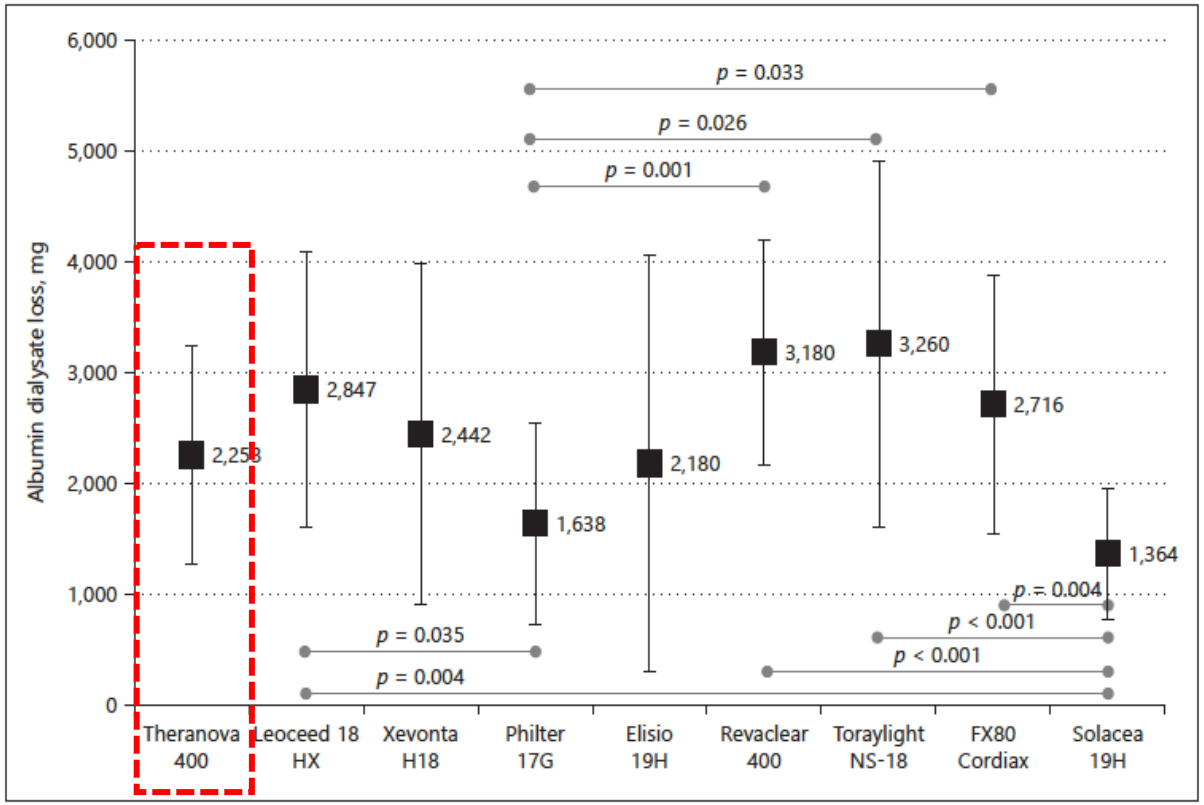
Cho NJ, et al. Long term effects of medium cut-off dialyzer on middle uremic toxins and cell-free emoglobin. PLOS One 2019; 14 (7): e0220448.

Alternativa a OL-HDF: Efficacia

Global Removal Score = ($urea_{RR}$+β2-m_{RR}, $myoglobin_{RR}$+ $prolactin_{RR}$+α1 $microglobulin_{RR}$+α1 acid $glycoprotein_{RR}$/6)– $albumin_{RR}$



Perdita di Albumina = MCO vs 8 filtri ad alto flusso per HDF – OL post diluizione (22 pazienti)



Patients (n) = 22

Age (yrs) = 63 ± 16

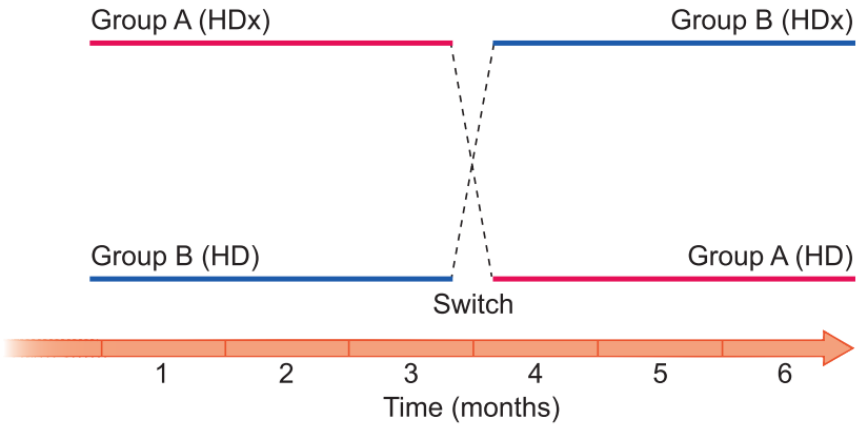
Dialysis age (mths) = 65 ± 74

Qb (ml/min) = 430 ± 40

Maduell F, et al. Medium cut-off dialyzer versus eight hemodiafiltration dialyzers: comparison using a global removal score. *Blood Purif 2019*

Riduzione Calcificazioni Vascolari

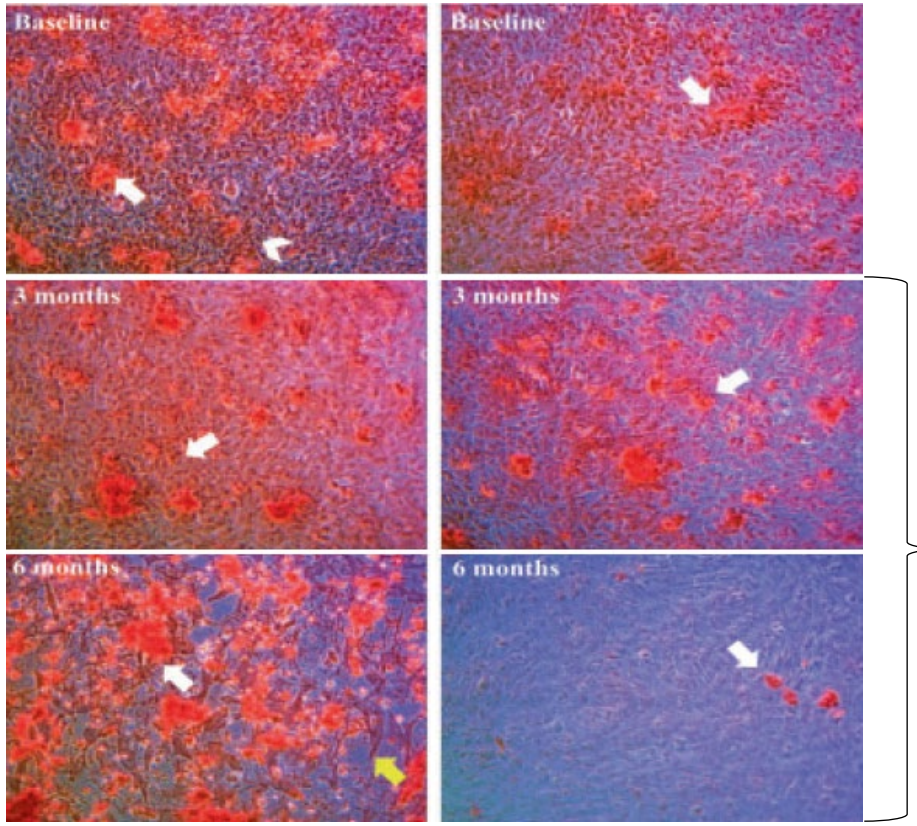
- **Studio Cross-Over**
- **20 pazienti HD cronica**
- **HDx vs. HD High-Flux.**
- **Follow-up = 3 mesi**
- **Prelievo sieri a 1, 2 e 3 mesi**
- **Test su VSMCs di ratto in vitro dopo stimolazione con Fosfato 3.3 micromolare**



1. **Quantificazione di depositi di calcio**
2. **Grado di Apoptosi e Necrosi (ELISA)**
3. **Livelli di induttori e inibitori della calcificazione**

Ciceri P., Cozzolino M., Pro-calcifying analysis of uraemic serum from patients treated with medium cut-off membrane in a prospective, cross-over study. *CKJ* 2021

Riduzione Calcificazioni Vascolari



HDx

HDx

Nel Gruppo HDx (membrana a MCO)

1. **Riduzione delle calcificazioni vascolari (15 - 32%).** Questo effetto si annullava al ritorno in HD
2. **Riduzione dei processi necrotici (58%)**
3. **Nessuna differenza** nei livelli di mediatori pro- e anti-calcificazione

Ciceri P., Cozzolino M., Pro-calcifying analysis of uraemic serum from patients treated with medium cut-off membrane in a prospective, cross-over study. *CKJ* 2021

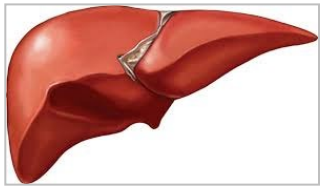
Perdita di Albumina

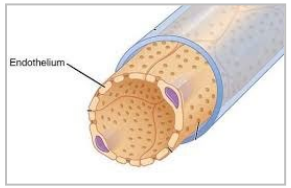
Table 1. Classification of hemodialysis membranes

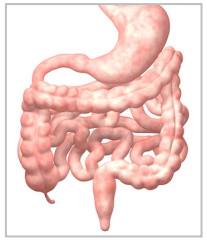
Category	Ultrafiltration coefficient[a] (mL/h/mmHg/m^2)	β_2-microglobulin clearance[b] (mL/min)	Albumin loss[c] (g)	Sieving coefficient[a]	
				β_2-microglobulin	Albumin
Low flux	<12	<10	0	–	0
High flux	14–40	20–40	<0.5	0.7–0.8	<0.01
MCO	40–60	>80	2–4	0.99	<0.01
Protein leaking	>40	>80	2–6	0.9–1.0	0.01–0.03
HCO	40–60	–	9–23	1.0	<0.2

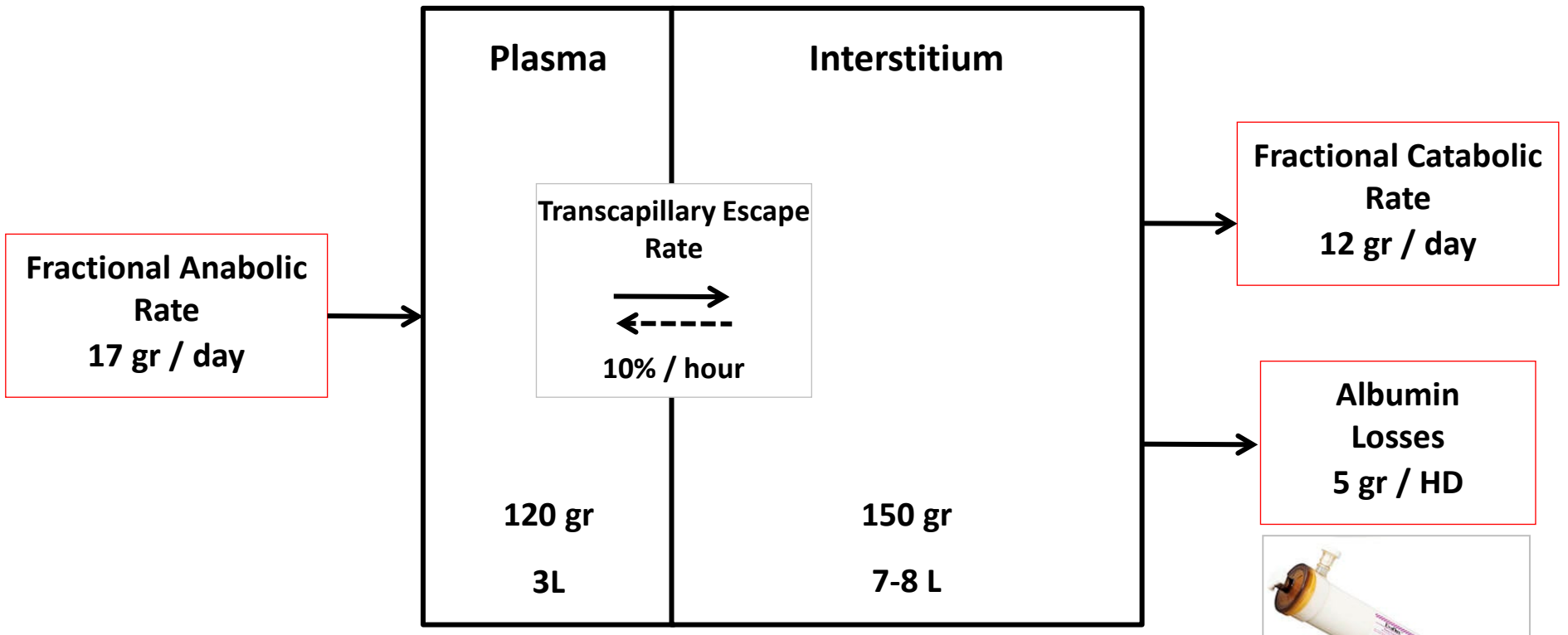
R.A. Ward et al. Hypoalbuminemia: a price worth paying for improved dialytic removal of middle-molecular-weight uremic toxins? *Nephrol Dial Transplant (2018)*

Perdita di Albumina









Rippe B, Öberg CM. Albumin Turnover in Peritoneal and Hemodialysis. *Semin Dial. 2016*

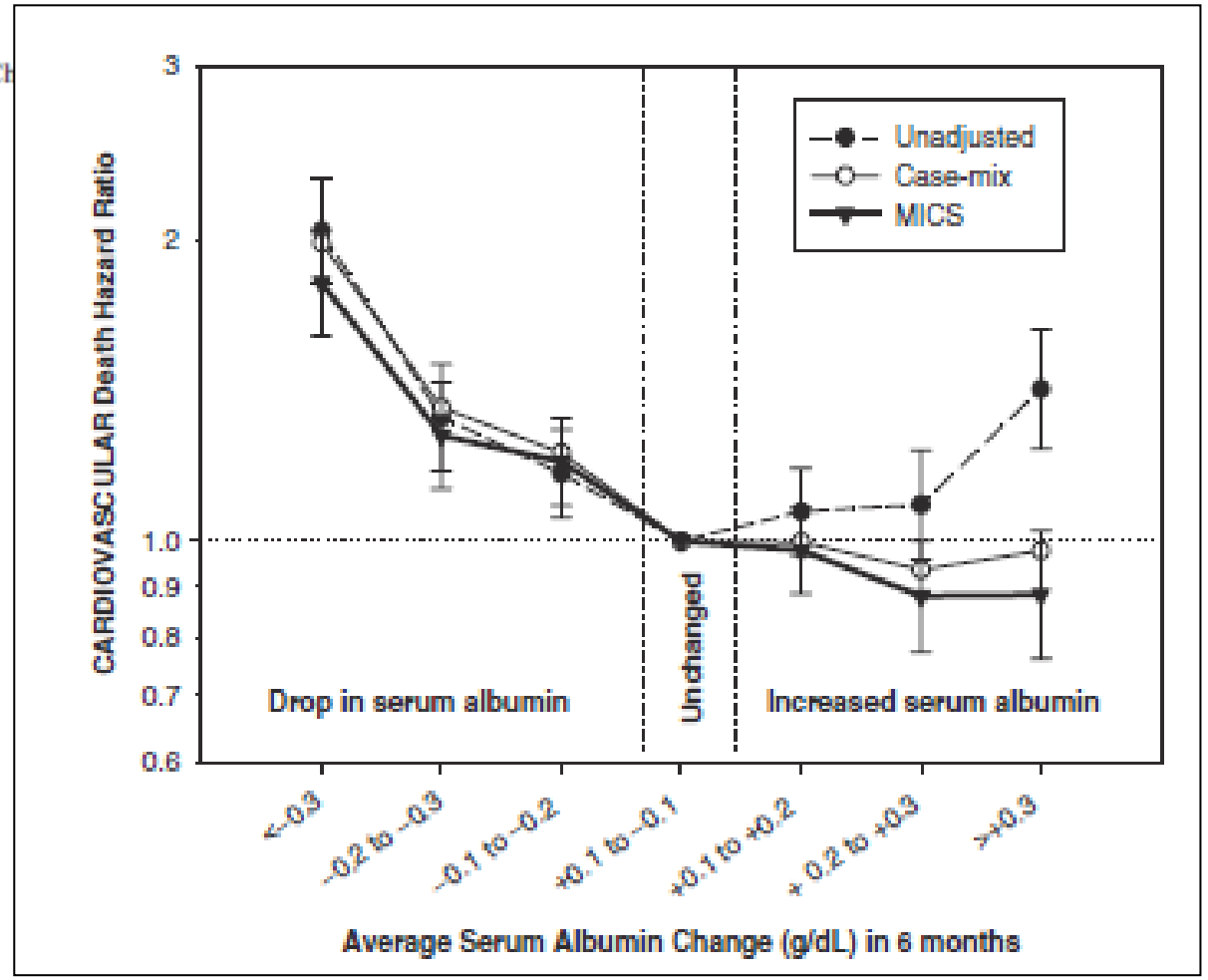
Nephrol Dial Transplant (2005) 20: 1880–1888
doi:10.1093/ndt/gfh941
Advance Access publication 14 June 2005

Original Article

Nephrology
Dialysis
Transplantation

Revisiting mortality predictability of serum albumin in the dialysis population: time dependency, longitudinal changes and population-attributable fraction

Kamyar Kalantar-Zadeh[1], Ryan D. Kilpatrick[1,2], Noriko Kuwae[1], Ch
Harry Alcorn Jr[4], Joel D. Kopple[1,2] and Sander Greenland[2]



Pazienti (n) = 58,058

Età (DS) = 60 ± 16 anni

Emodialisi Cronica

Follow-up = 2 anni

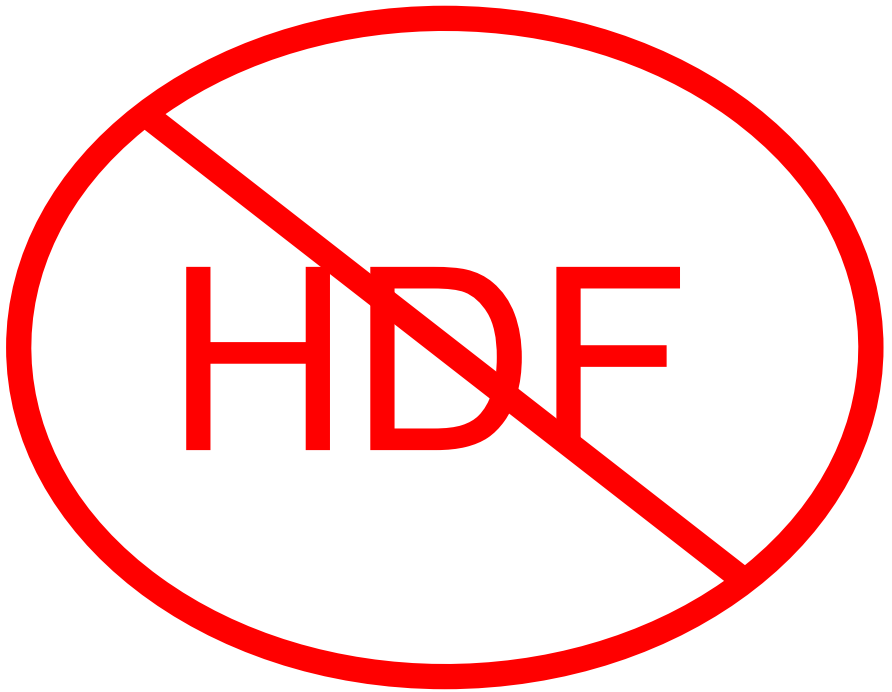
Perdita di Albumina

Possibili benefici di una perdita moderata:

- Rimozione di tossine legate all'albumina
- Rimozione forme modificate di albumina (carbamilata, glicosilata etc.)
- Stimolo a nuova produzione epatica

R.A. Ward et al. Hypoalbuminemia: a price worth paying for improved dialytic removal of middle-molecular-weight uremic toxins? *Nephrol Dial Transplant (2018)*

Perdita di Albumina



R.A. Ward et al. Hypoalbuminemia: a price worth paying for improved dialytic removal of middle-molecular-weight uremic toxins? *Nephrol Dial Transplant (2018)*

2

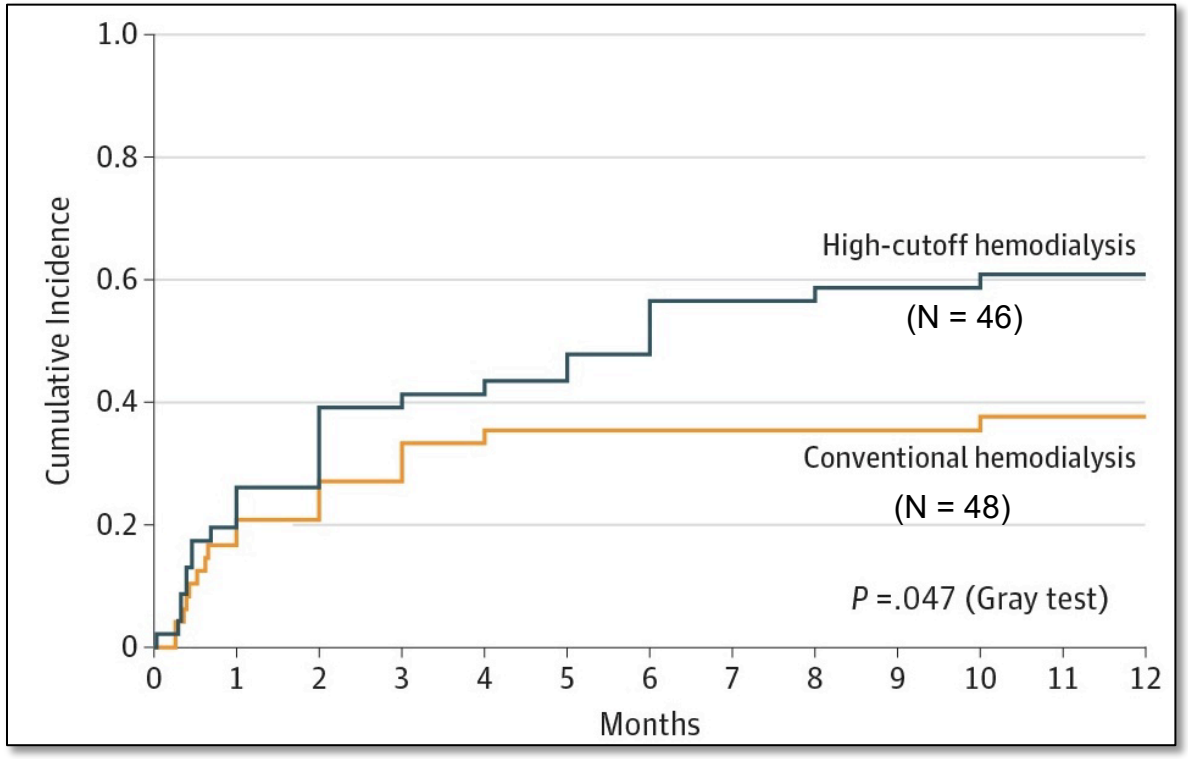
INDICAZIONI

ALTO CUT-OFF

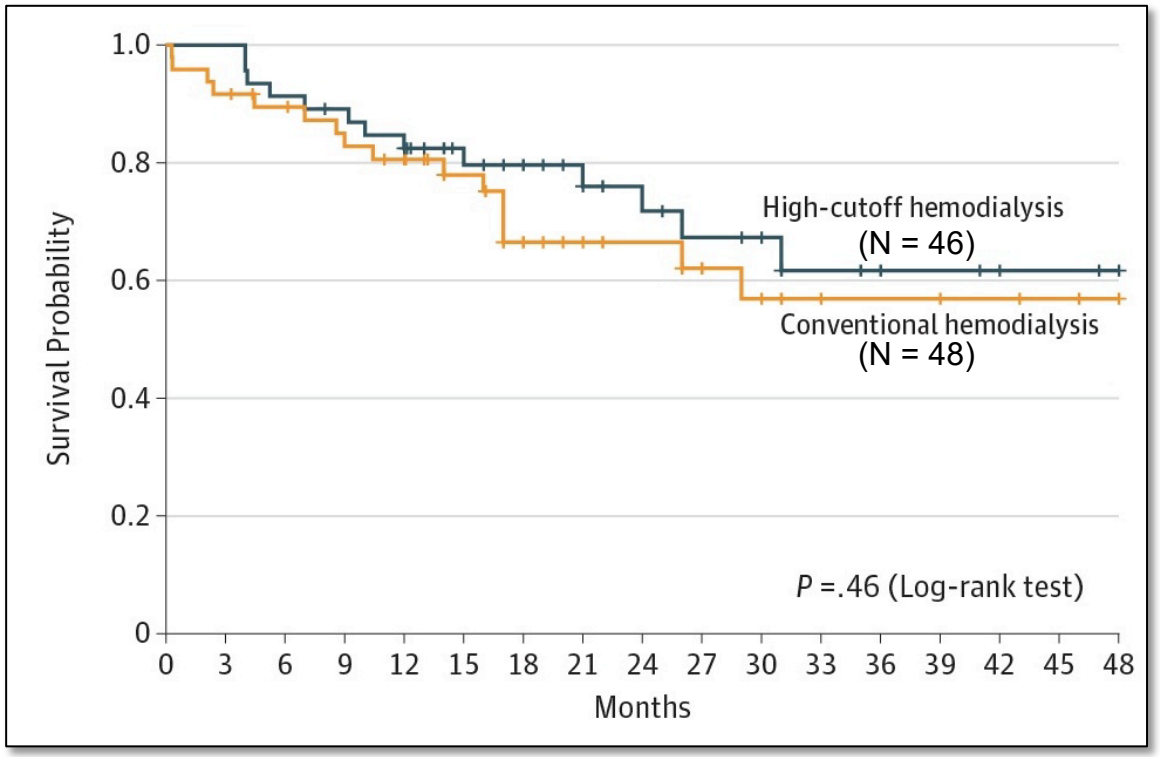
- Mieloma
- Sepsi
- Resistenza all’Eritropoietina

Mieloma - MYRE

Dialysis Independence



Patient Survival



- **94 pts with Myeloma Cast Nephropathy**
- **Free Light Chains >500 mg/L (Freelite™)**
- **Acute Kidney Injury requiring Dialysis**

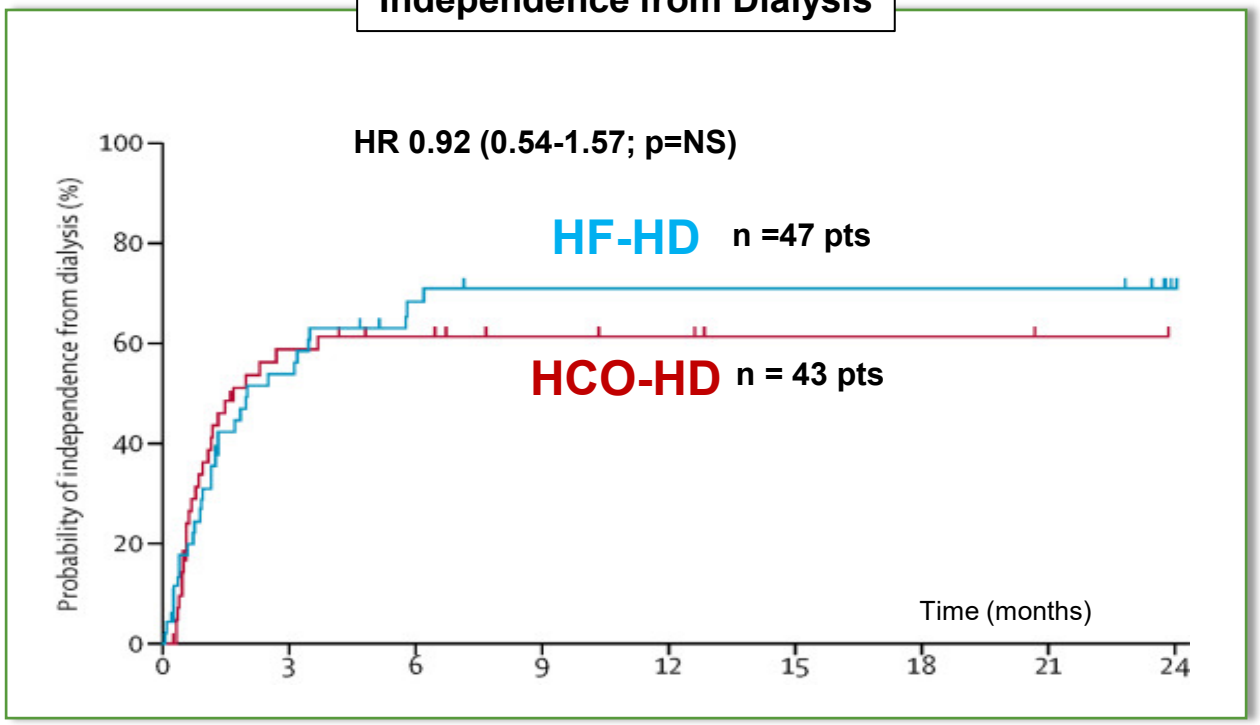
- **8 HD , 5-hour duration, 10 days**

- **3 additional HD/ week, 3 cycles of chemotherapy**

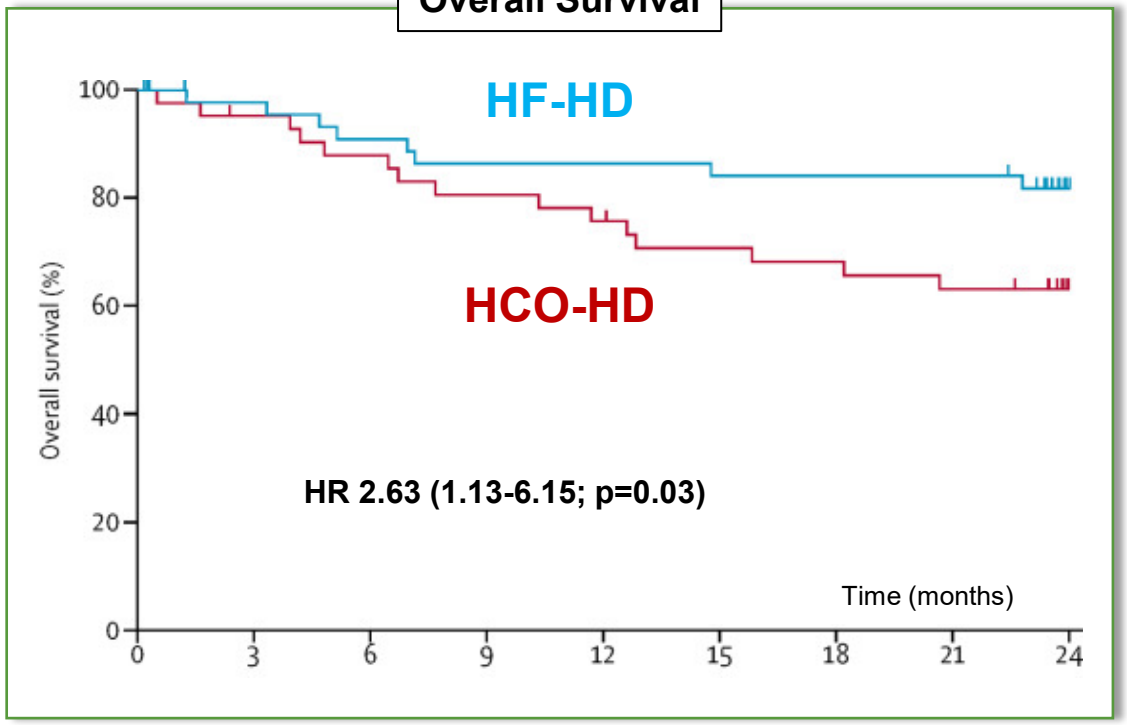
Bridoux F et al. MYRE Study Group, JAMA 2017; 318 (21): 2099-2110

Mieloma - EuLite

Independence from Dialysis



Overall Survival



- **90 pts with Myeloma Cast Nephropathy**
- **Free Light Chains >500 mg/L (Freelite™)**
- **Acute Kidney Injury requiring Dialysis**

- **7 HD-HCO , 8-hour duration, 12 days**
- **3 HD-HCO / week, 6/8-hour duration, 90 days**

Hutchison CA et al. EULITE Trial. Lancet Haematol 2019; 6: e217-228.

Studio HICOSS (High Cut Off Sepsis Study)

Shock Settico con Insufficienza Renale Acuta (n)= 81

Randomizzazione

Membrana ad Alto Flusso

5 Giorni - CVVHD

Qb 150-200 ml/min

Qd 35 ml/Kg/h

Membrana ad Alto Cut Off

5 Giorni - CVVHD

Qb 150-200 ml/min

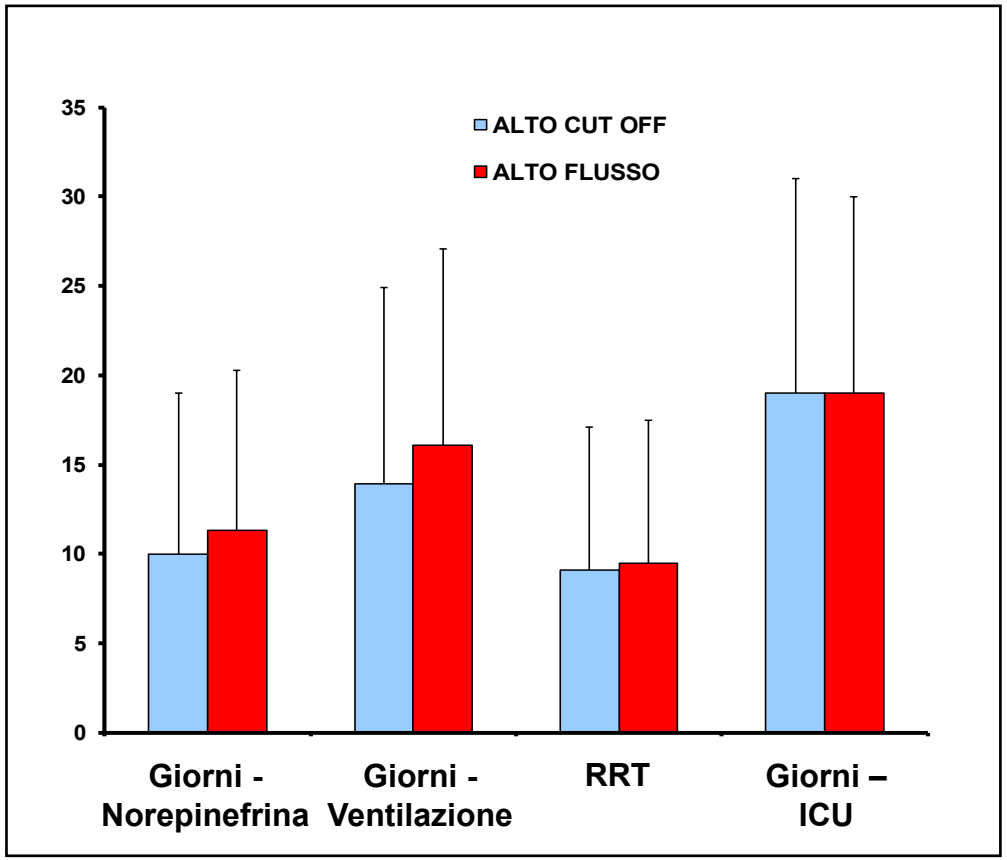
Qd 35 ml/Kg/h

a) Riduzione del 50% della Dose di Catecolamine

b) Miglioramento clinico (SOFA), perdita di albumina

Mortalità a 28 giorni: 33% vs 31%

Honoré et al. Proc. 10th World Federation of Societies of Intensive and Critical Care Meeting, Firenze, 2009.

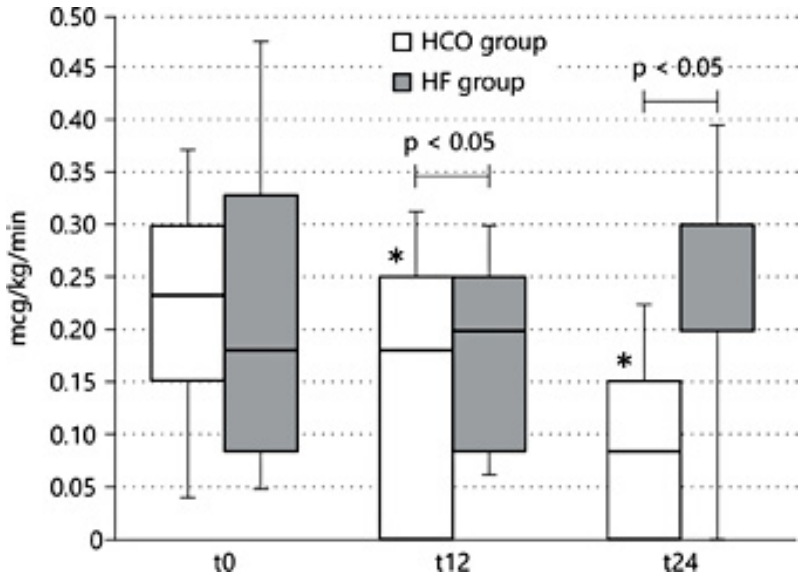


Hemodialysis with High Cut-Off Hemodialyzers in Patients with Multi-Drug Resistant Gram-Negative Sepsis and Acute Kidney Injury: A Retrospective, Case-Control Study

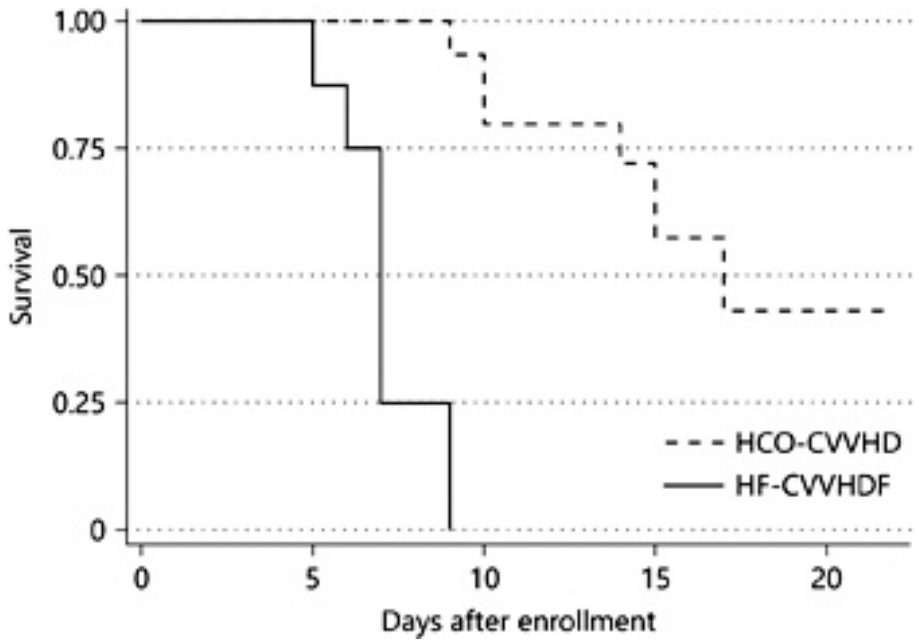
Cosimo Chelazzi[a, b] Gianluca Villa[a, b] Maria Grazia D'Alfonso[c]
Paola Mancinelli[a, b] Guglielmo Consales[e] Margherita Berardi[d]
Angelo Raffaele De Gaudio[a, b] Stefano Romagnoli[a, b]

- **AKI e Sepsi da GRAM ⁻**
- **26 pazienti (HCO CVVHD 16 vs HF-CVVHDF 8)**
- **Riduzione giorni di ventilazione meccanica e uso di inotropi**
- **Riduzione mortalità in Terapia Intensiva (P=0,03) ma non mortalità in ospedale totale**

Uso di Inotropi



Sopravvivenza



Blood Purif. 2016; 42: 186-193

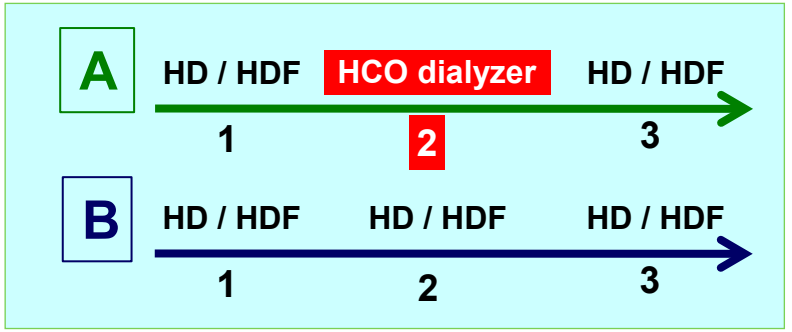
HCO and ESA Resistance

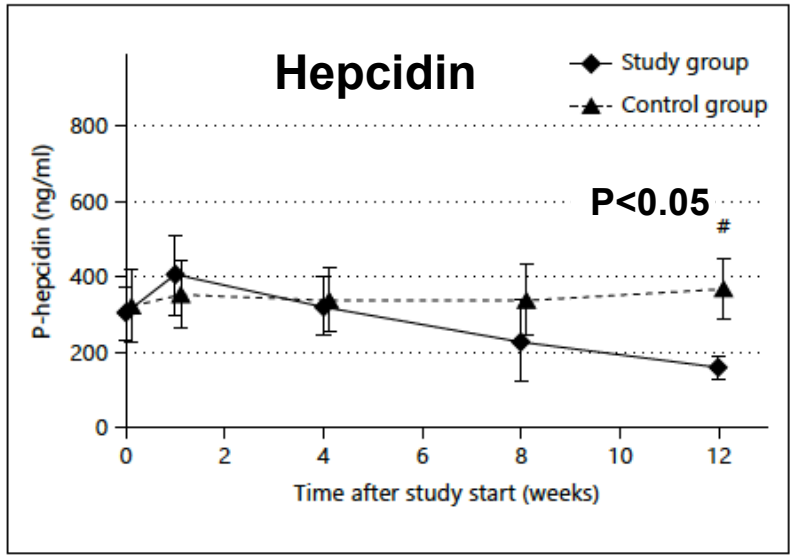
Patients (n) = 24

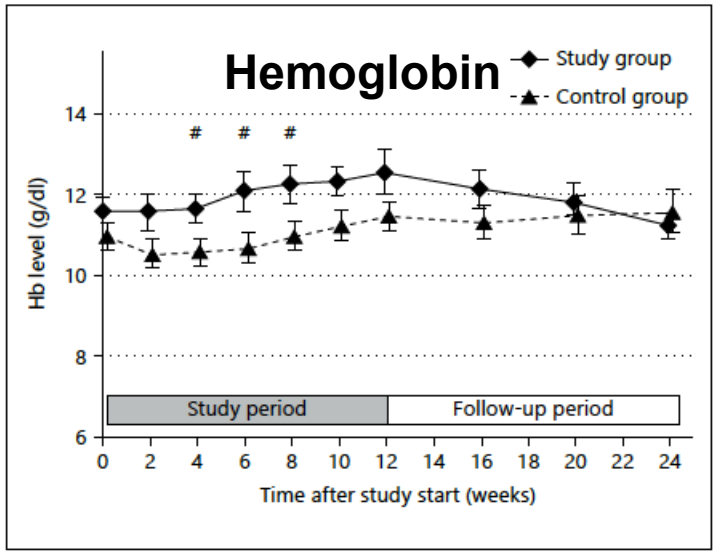
Age (yrs) = 65 ± 14

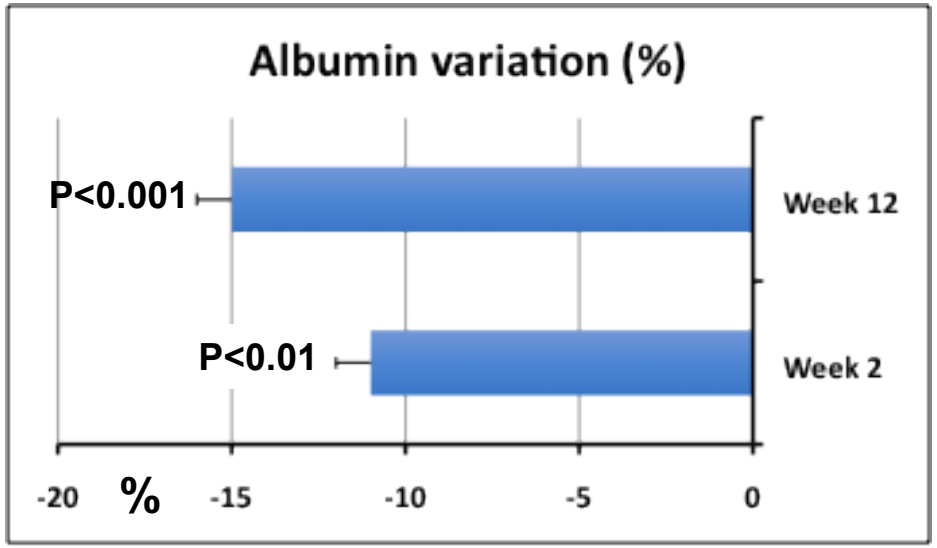
HD / HDF = 18 / 6

Follow-up = 12 weeks









Teatini U et al. Blood Purif 2016; 41: 80-86

TAKE HOME MESSAGES

01 Nuova distribuzione dei pori = nuovo range di cut-off

02 Le membrane MCO sono sicure ed efficaci.

03 Le membrane MCO permettono di migliorare le performances di HD ad alto flusso

04 Le membrane ad Alto Cut-Off sembrano avere uso meno suffragato da trials

GRAZIE DELL’ATTENZIONE

Sepsi

Blood Purification

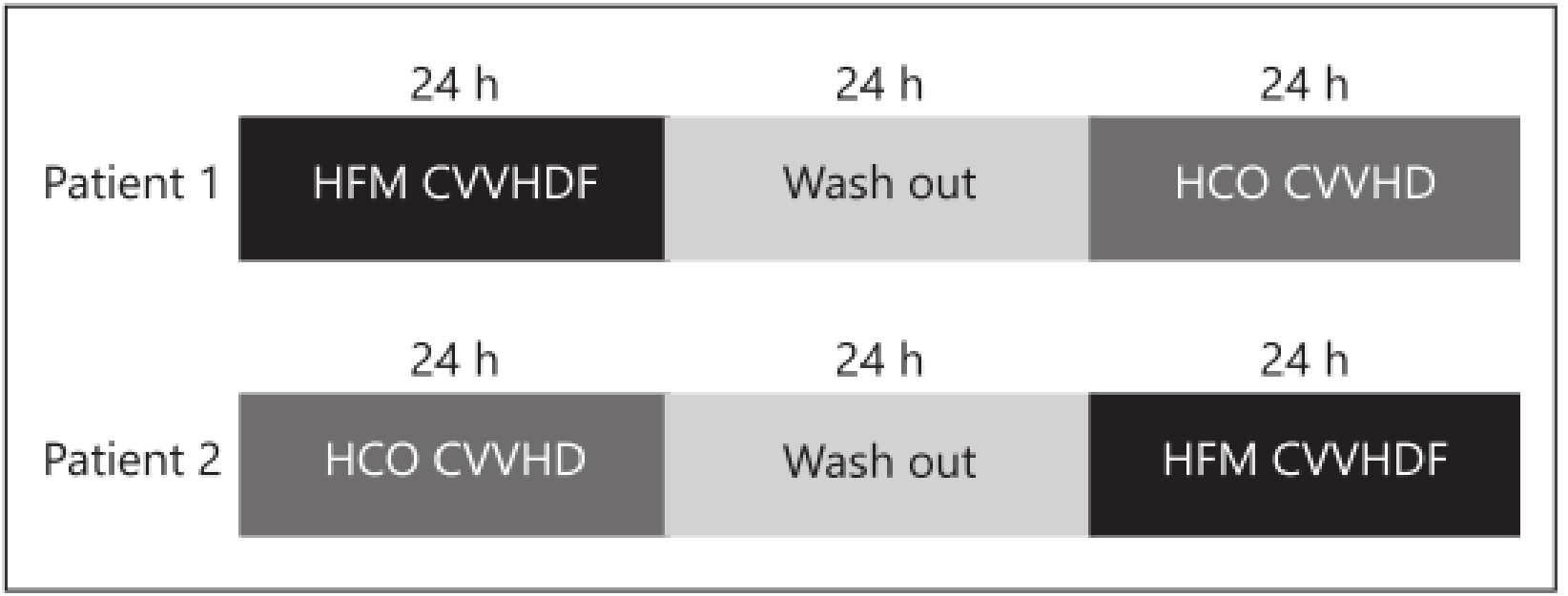
Blood Purif 2018;46:248–256
DOI: 10.1159/000489082

Continuous Veno-Venous High Cut-Off Hemodialysis Compared to Continuous Veno-Venous Hemodiafiltration in Intensive Care Unit Acute Kidney Injury Patients

Sanjeet Balgobin[a, b] Marion Morena[c] Vincent Brunot[a] Noemie Besnard[a] Delphine Daubin[a] Laura Platon[a] Romaric Larcher[a, c] Laurent Amigues[a] Liliane Landreau[a] Anne-Sophie Bargnoux[c, d] Anne-Marie Dupuy[d] Jean-Paul Cristol[c, d] Kada Klouche[a, c]

[a]Department of Intensive Care Medicine, Montpellier University Hospital, Montpellier, France; [b]Department of nephrology, Clinique Médipole, Perpignan, France; [c]PhyMedExp, INSERM, CNRS, University of Montpellier, Montpellier, France; [d]Department of Biochemistry and Hormonology, Montpellier University Hospital, Montpellier, France

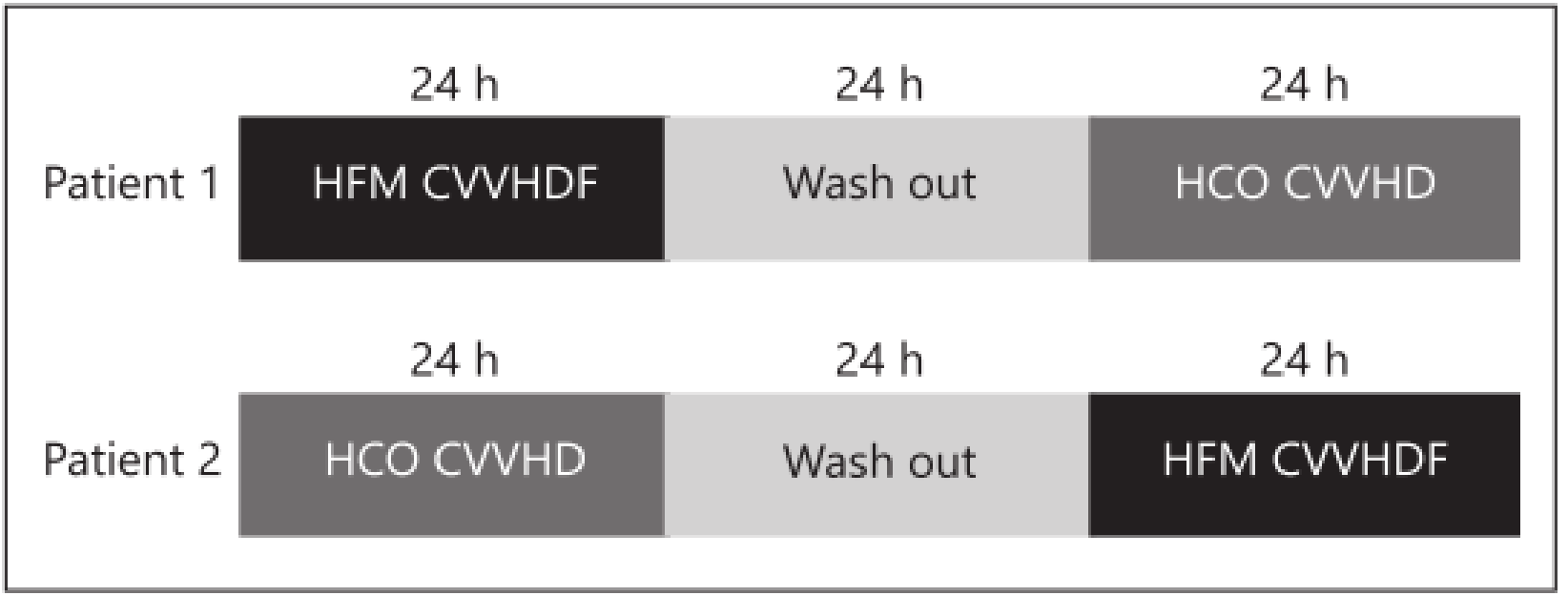
Sepsi



10 pazienti totali con AKI e necessità di trattamento extracorporeo, randomizzati a uno dei due schemi sopra descritti.

- <u>7 pazienti con AKI SETTICA</u>
- 2 pazienti con AKI ISCHEMICA
- 1 paziente con AKI

Sepsi



- **Stessa clearance beta2m** con flusso dialisato più basso (2 vs 4 L/h) e **meno episodi ipotensivi**
- Non perdite significative di **albumina**
- Non aumento di produzione di citochine pre-infiammatorie

FX

XEVONTA

ELISIO H

Etc…

Table 1. Classificati

Category
Low flux
High flux
MCO
Protein leaking
HCO

THERALITE

THERANOVA

Table 1. Classification of hemodialysis membranes

Category	Ultrafiltration coefficient[a] (mL/h/mmHg/m^2)	β_2-microglobulin clearance[b] (mL/min)	Albumin loss[c] (g)	Sieving coefficient[a]	
				β_2-microglobulin	Albumin
Low flux	<12	<10	0	–	0
High flux	14–40	20–40	<0.5	0.7–0.8	<0.01
MCO	40–60	>80	2–4	0.99	<0.01
Protein leaking	>40	>80	2–6	0.9–1.0	0.01–0.03
HCO	40–60	–	9–23	1.0	<0.2

R.A. Ward et al. Hypoalbuminemia: a price worth paying for improved dialytic removal of middle-molecular-weight uremic toxins? *Nephrol Dial Transplant (2018)*

Dalla Teoria…

1

INDICAZIONI

OL-HDF non applicabile per:

A. Accesso vascolare con Q_B < 250 ml/min

B. FAV di recente confezionamento (aghi < 16 G)

C. Elevato numero di comorbidità

D. Rischio elevato di coagulazione del filtro

Davenport A. Dialysis and Patient Factors Which Determine Convective Volume Exchange in Patients Treated by Postdilution Online Hemodiafiltration *Artif. Organs 2016*