The 19th International Congress of Nephrology, Dialysis and Transplantation (ICNDT)

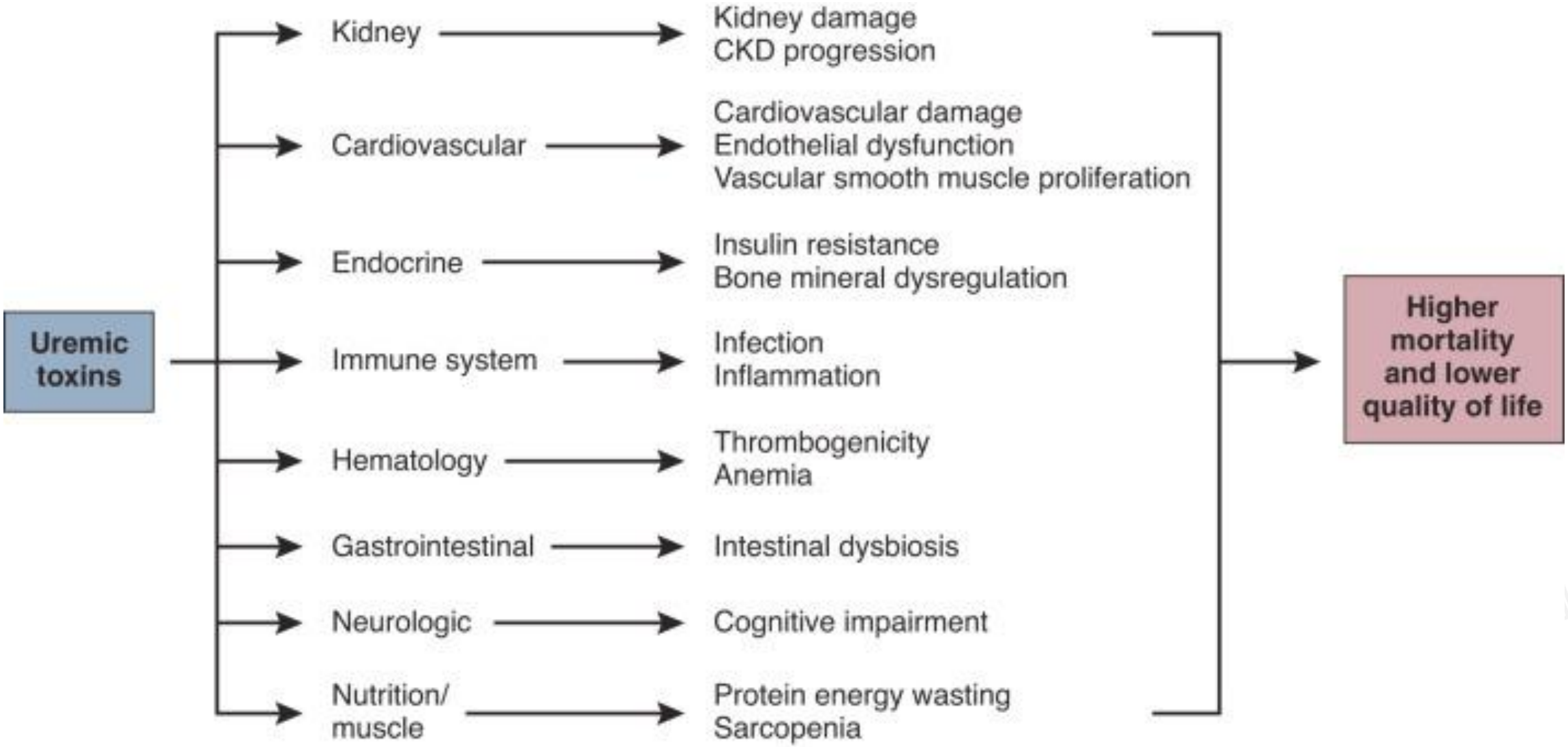
12-15 December 2023
Homa Hotel, Tehran

Use of High & Medium Cut-Off Dialyzers

Samimagham HR .MD

Professor of Nephrology Of HUMS

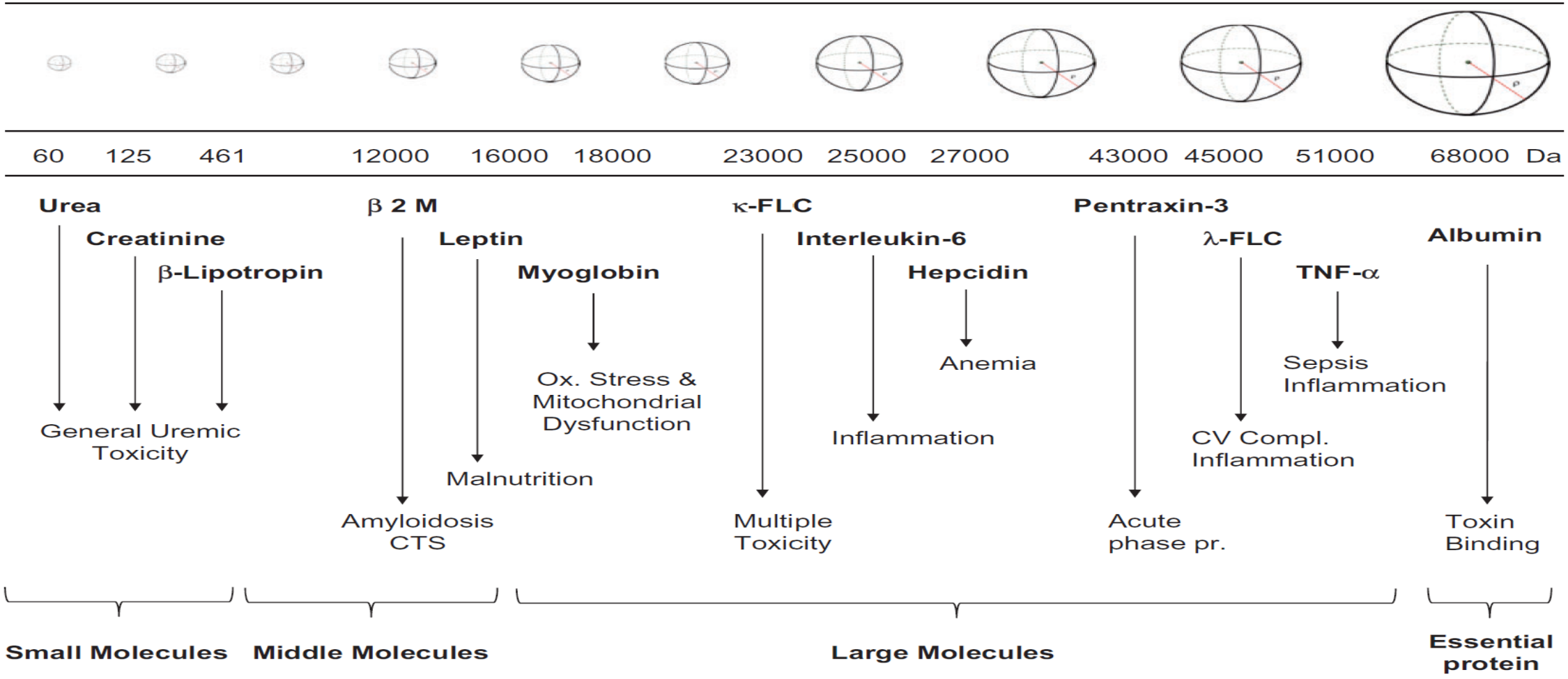
Hemodialysis Therapy: A Never-Ending Journey


Uremic toxins
Kidney
Kidney damage
CKD progression
Cardiovascular
Cardiovascular damage
Endothelial dysfunction
Vascular smooth muscle proliferation
Endocrine
Insulin resistance
Bone mineral dysregulation
Immune system
Infection
Inflammation
Hematology
Thrombogenicity
Anemia
Gastrointestinal
Intestinal dysbiosis
Neurologic
Cognitive impairment
Nutrition/ muscle
Protein energy wasting
Sarcopenia
Higher mortality and lower quality of life

New Uremic Toxin Classification

Uremic toxin source	Molecular characteristics	Prototype uremic toxin
Exogenous	Gut-derived, protein-bound <80%	homocysteine, indoxyl sulfate, paracresyl sulfate, carboxymethyl lysine, and kynurenines
	Gut-derived, protein-bound ≥80%	Hcy, IS, pCS, CML, kynurenines
Endogenous Water-soluble	Small molecules <0.5 kDa	ADMA, SDMA, uric acid, carbamylated compounds, urea, TMAO
	Small-middle molecules 0.5–15 kDa	β2-microglobulin, IL-8
	Medium-middle molecules >15–25 kDa	TNF, IL-18, IL-10, IL-6, kappa-FLC, myoglobin, sTNFR2, FGF-2, prolactin, complement factor D
	Large-middle molecules >25–58 kDa	Pentatraxin-3, sTNFR1, AGEs, FGF-23, lambda-FLC, CX3CL1, CXCL12, IL-2, YKL-400
	Large molecules >58–170 kDa	Albumin

Schematic representation of different classes of uremic toxins with their molecular size and relevant clinical effects.



Where are we?

Uremic toxin clearance based on the dialyzer characteristics

Uremic toxin source	Molecular characteristics	Prototype uremic toxin	Low-flux HD	High-flux HD	High-flux HDF	Medium cutoff HD	High cutoff HD
Exogenous	Gut-derived, protein-bound <80%	homocysteine, indoxyl sulfate, paracresyl sulfate, carboxymethyl lysine, and kynurenines	✓	✓	✓	✓	✓
	Gut-derived, protein-bound ≥80%	Hcy, IS, pCS, CML, kynurenines		✓	✓	✓	✓
Endogenous Water-soluble	Small molecules <0.5 kDa	ADMA, SDMA, uric acid, carbamylated compounds, urea, TMAO	✓	✓	✓	✓	✓
	Small-middle molecules 0.5–15 kDa	β2-microglobulin, IL-8		✓	✓	✓	✓
	Medium-middle molecules >15–25 kDa	TNF, IL-18, IL-10, IL-6, kappa-FLC, myoglobin, sTNFR2, FGF-2, prolactin, complement factor D			✓	✓	✓
	Large-middle molecules >25–58 kDa	Pentatraxin-3, sTNFR1, AGEs, FGF-23, lambda-FLC, CX3CL1, CXCL12, IL-2, YKL-400				✓	✓
	Large molecules >58–170 kDa	Albumin					✓

Routine HD

Routinely employed filters for chronic defined as high-flux (HF) allow diffusive and convective clearances, having polyarylethersulfone (PAES) as its main compound.

The mean pore radius of these filters is 3.9 nm, and they can be applied in conventional HD (high-flux HD [HF-HD]), or hemodiafiltration (high-flux hemodiafiltration [HFHDF]).

The HF-HD modality is limited in removing solutes with molecular weight greater than 15 kDa.

HF-HDF modality

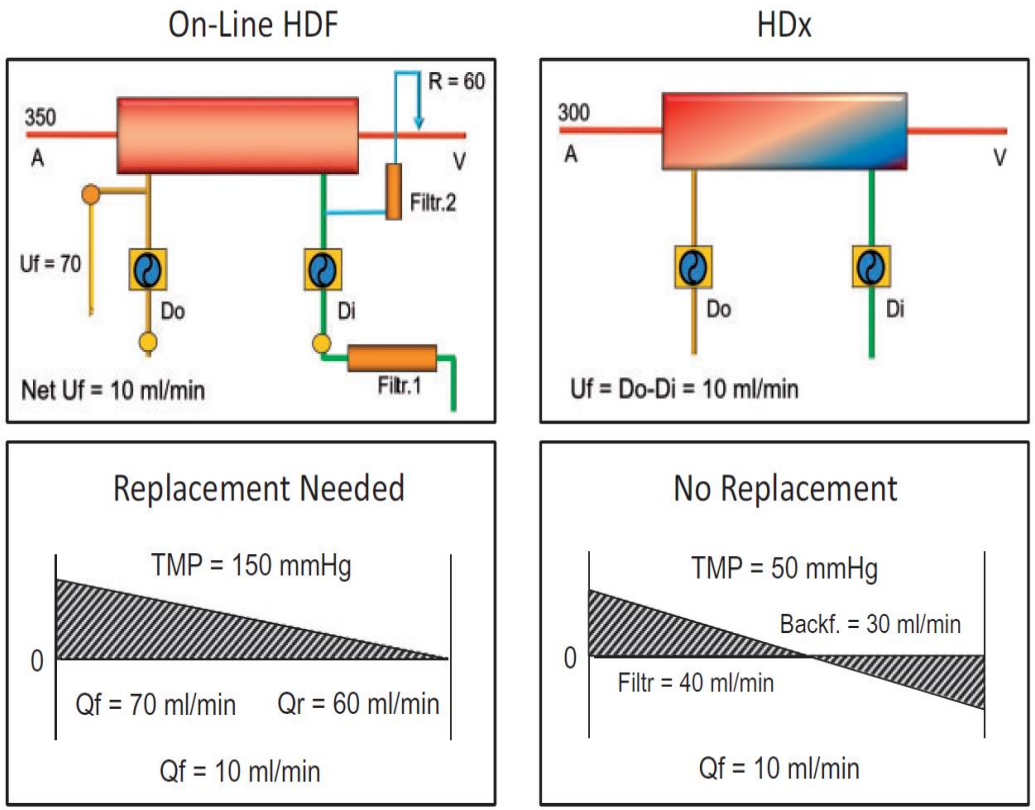
Even utilizing the same membrane as in HFHD, the online HF-HDF modality removes efficiently a broader range of molecules up to 25 kDa, thanks to high ultrafiltration volumes of around 100 mL/min, which represent the convective clearance.

During a four-hour HF-HDF session, desirably 21 L or more of ultrafiltrate are generated, reinfusion volume 19 L, at the end of the session the patient will have a reduction of 2 kg (~2 L) in his body mass.

EXPANDED HD(HDx)

The term expanded HD (HDx) has been proposed to define a treatment where diffusion and convection are conveniently combined inside a hollow fiber dialyzers equipped with an MCO membrane.

EXPANDED HD



In HDx, the convection flow is maintained by internal filtration but it is compensated by the mechanism of back filtration inside the filter.

The special configuration of the MCO membrane with reduced inner diameter allows for high rates of internal filtration and back filtration.

Concept	Definition
Sieving coefficient	The ratio between the solute concentration in the filtrate and the solute concentration in plasma water in the absence of a diffusion gradient across the membrane
Molecular weight retention onset	MW at which the sieving coefficient first reaches 0.9 (90%), the extraction from the blood of molecules with higher MW than the retention onset is 90% or less
Molecular weight cutoff	MW at which the sieving coefficient reaches 0.1 (10%), the extraction from the blood of molecules with higher MW than the cutoff is 10% or less
Reduction ratio	Subtraction of the pre-HD session concentration from the post-HD session concentration of a solute, divided by its pre-HD session concentration
Backfiltration/Internal filtration	Inflow of fluids across the dialysis membrane, from the dialysate compartment towards the blood compartment

HD, hemodialysis; MW, molecular weight.

Core concepts and their definitions regarding HD membranes

MCO membranes

- ✓Internal filtration between 30 and 50 mL/min combined with the sieving characteristics of MCO membranes allows for convective clearance values of medium-large molecules equal or even superior to those achieved in high-volume online HDF, without the need for fluid replacement and very high filtration fractions inside the hemodialyzer.

- ✓Blood flow 300 mL/min and dialysate flow 500 mL/min are sufficient to achieve optimal clearance in the system .

Blood Purif. 2021, 51, 138–146.

Medium or High cut-off membranes

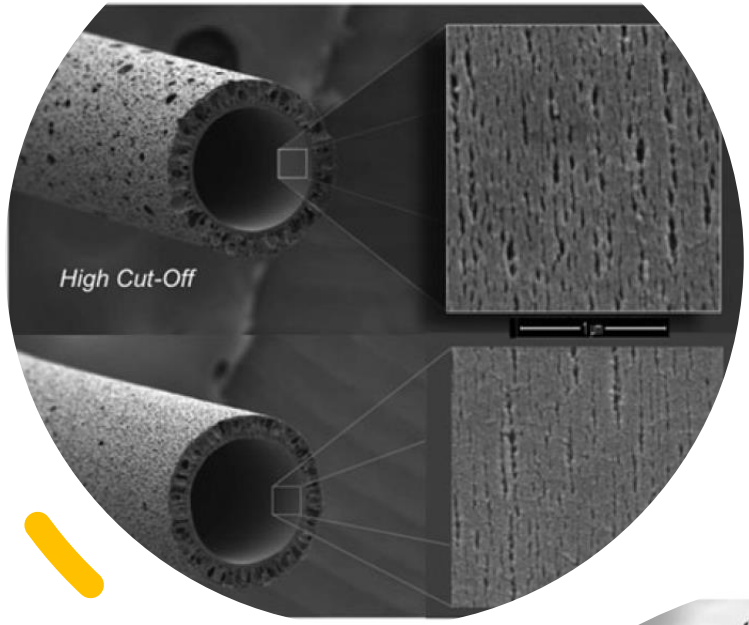
Medium or high cut-off membranes have recently been introduced in the clinical practice.

These membranes are usually composed of polyarylethersulfone and polyvinylpyrrolidone, reaching a surface area of at least 1.6 m 2 (the most commonly employed are Theranova 400 and Theranova 500, with an effective surface area of 1.7 m and 2.0 m 2 , respectively.

Four dialyzer types in parameter characteristics

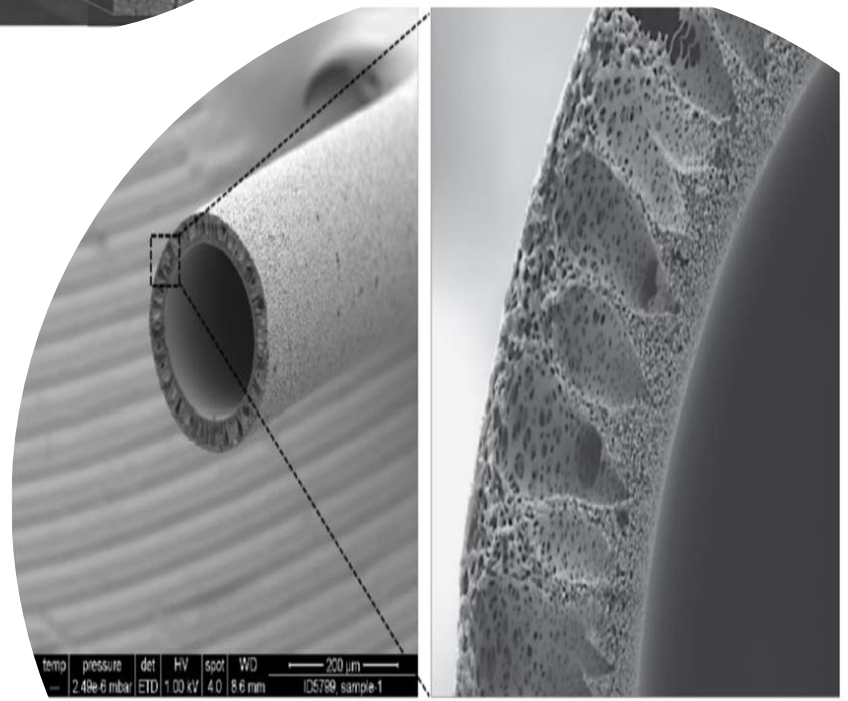
Device	Membrane Type	Structural Characteristics				
		Pore Radius * (nm)	Fiber Inner Diameter (μm)	Fiber Wall Thickness (μm)	Effective Surface Area (m^2)	UF-Coefficient ** (mL/h/mmHg)
Pollyflux 17L	Low-flux	3.1 ± 0.2	215	50	1.7	12.5
Revaclear 400	High-flux	3.9 ± 0.1	190	35	1.8	54
Theranova 400	Medium cut-off	5.0 ± 0.1	180	35	1.7	48
Theranova 500	Medium cut-off	5.0 ± 0.1	180	35	2.0	59
Theralite 2100	High cut-off	10.0 ± 2.0	215	50	2.1	52

Disruptive technology



The technology employed for the development of **medium cutoff (MCO)** and **high cutoff (HCO)** dialyzers is disruptive since it provides equivalent or even higher removal of middle molecules in the conventional HD modality than HF-HDF modality without the need for a devoted hemodiafiltration (HDF) machine and the production of online reinfusion solution.

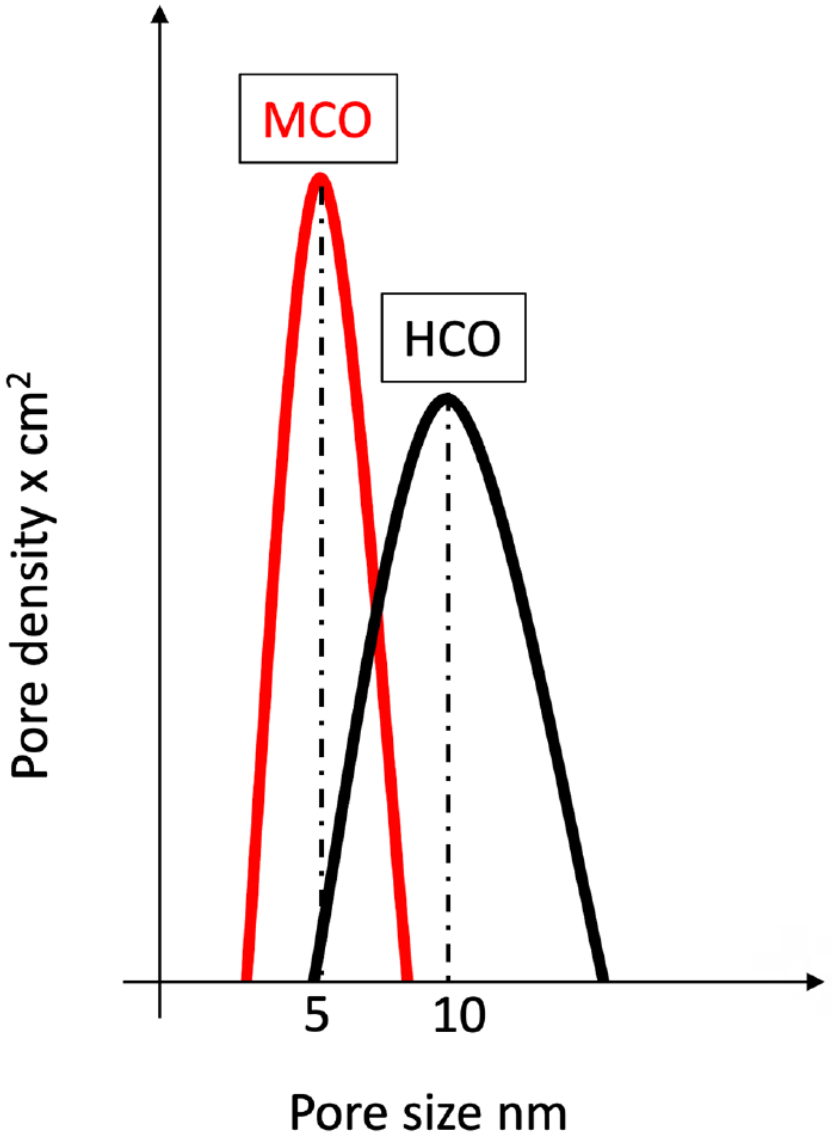
- Hemodiafiltration for Small- and Middle-Sized Molecules Clearance? Blood Purif. 2019;47(1–3):126–31.



Scanning electron micrographs of fiber (**left**) and fiber wall (**right**). Pictures are from Baxter [1] Inc., Deerfield, IL, USA.

Pore size distribution of medium cutoff (MCO) and high cutoff (HCO) membranes.

- The MCO membrane mean pore radius is 5 nm, standard deviation 0.1 nm.
- The HCO membrane mean pore radius is 10 nm, standard deviation 2.0 nm.



Braz. J. Nephrol. (J. Bras. Nefrol.) 2021;43(3):410-416

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Use of High & Medium Cut-Off Dialyzers

Can use these dialyzers in maintenance hemodialysis patients and CKRT?

TEHRAN 2023

The Effect of Expanded Hemodialysis on Uremic Toxins Removal

- Dialysis Adequacy(spKt/V from 1.62 at baseline to 1.70)
- Removal of b2 Microglobulin (b2-M)
- Removal of Free Light Chains (FLCs) and Other Middle Molecules(higher myoglobin)
- Removal of Protein-Bound Uremic Toxins (PBUTs)such as homocysteine, indoxyl sulfate (IS) and p-cresulfate (p-CS)

Uremic toxin source	Molecular characteristics	Prototype uremic toxin	Low-flux HD	High-flux HD	High-flux HDF	Medium cutoff HD	High cutoff HD
Exogenous	Gut-derived, protein-bound <80%	homocysteine, indoxyl sulfate, paracresyl sulfate, carboxymethyl lysine, and kynurenines	✓	✓	✓	✓	✓
	Gut-derived, protein-bound ≥80%	Hcy, IS, pCS, CML, kynurenines		✓	✓	✓	✓
Endogenous Water-soluble	Small molecules <0.5 kDa	ADMA, SDMA, uric acid, carbamylated compounds, urea, TMAO	✓	✓	✓	✓	✓
	Small-middle molecules 0.5–15 kDa	β2-microglobulin, IL-8		✓	✓	✓	✓
	Medium-middle molecules >15–25 kDa	TNF, IL-18, IL-10, IL-6, kappa-FLC, myoglobin, sTNFR2, FGF-2, prolactin, complement factor D			✓	✓	✓
	Large-middle molecules >25–58 kDa	Pentatraxin-3, sTNFR1, AGEs, FGF-23, lambda-FLC, CX3CL1, CXCL12, IL-2, YKL-400				✓	✓
	Large molecules >58–170 kDa	Albumin					✓

In conclusion, expanded hemodialysis with MCO membranes showed a greater capacity to remove middle-molecule toxins than high-flux dialysis.

HCO membrane in continuous kidney replacement therapy (CKRT)

A well-established use for the HCO membrane is in continuous kidney replacement therapy (CKRT), precisely for continuous veno-venous hemodialysis (CVVHD).

- ✓Weidhase et al. proved in a randomized trial with 60 individuals that the clearances of ß2-microglobulin (12 kDa), myoglobin (17 kDa), and interleukin 6 (26 kDa) were higher in the group that carried out CVVHD with HCO membrane versus the group that carried out CVVHD with HF membrane. PLoS ONE. 2019 Apr;14(4):e0215823.

HCO membrane
in continuous kidney replacement therapy (CKRT)

There was no difference in albumin losses

Low albumin loss may be occurred secondary to low blood flow.

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EDITORIAL

Open Access

Medium cut-off membranes - closer to the natural kidney removal function

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Special MCO membranes should raise the standard of treatment available for all chronic HD patients, potentially decrease inflammatory responses, and generally, improve patient outcomes.

The Effect of Expanded Hemodialysis on Inflammation

Year	First Author	Patients (N)	Dialysis Treatment	Time	Study Design	Cytokines Significantly Removed by MCO Pre-Post Dialysis	Cytokines Significantly Removed by MCO at End of Study Period	Cytokines Removed by MCO Pre-Post Dialysis but No Significance
2017	Zickler	48	HD MCO vs. HF	12 weeks	4-week MCO 4-week HF pre-post dialysis 8-week extension	TNF-α mRNA IL-6 mRNA sTNFR1	TNF-α mRNA IL-6 mRNA sTNFR1	-
2019	Belmouaz	40	HD MCO vs. HF	6 months	3-month MCO 3-month HF pre-post dialysis	Homocysteine	Homocysteine	IL-1b, IL-6, TNF-a, Ox-LDL, 8-iso-Prostaglandin F2a, SOD activity
2019	Cozzolino	20	HD MCO vs. HF	6 months	3-month MCO 3-month HF pre-post dialysis	-	-	IL-1b, IL-6, TNF-α
2020	Lim	49	HD MCO vs. HF	12 weeks	12 weeks	TNF-α	TNF-α	-
2020	Sevinc	52	HD MCO vs. HF	6 months	3-month MCO 3-month HF pre-post dialysis	VEGF	VEGF	FGF-23, IFN-γ, IL-6, IL-10, IL-17A
2020	Weiner	172	HD MCO vs. HF	24 weeks	24 weeks	TNF-α	TNF-α	IL-6
2020	Yeter	42	HD MCO vs. HF vs. LF	6 months	6 months	-	-	TOS, TAS, PON-1, CRP

NDT Advance Access published September 1, 2016

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doi: 10.1093/ndt/gfw310

ndt
Nephrology Dialysis Transplantation

Original Article

Performance of hemodialysis with novel medium cut-off dialyzers

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MCO HD removes a wide range of middle molecules more effectively than high-flux HD and even exceeds the performance of high-volume HDF for large solutes, particularly λFLC.

Medium cut-off dialyzer for middle molecular uremic toxins in AKI and CKD settings

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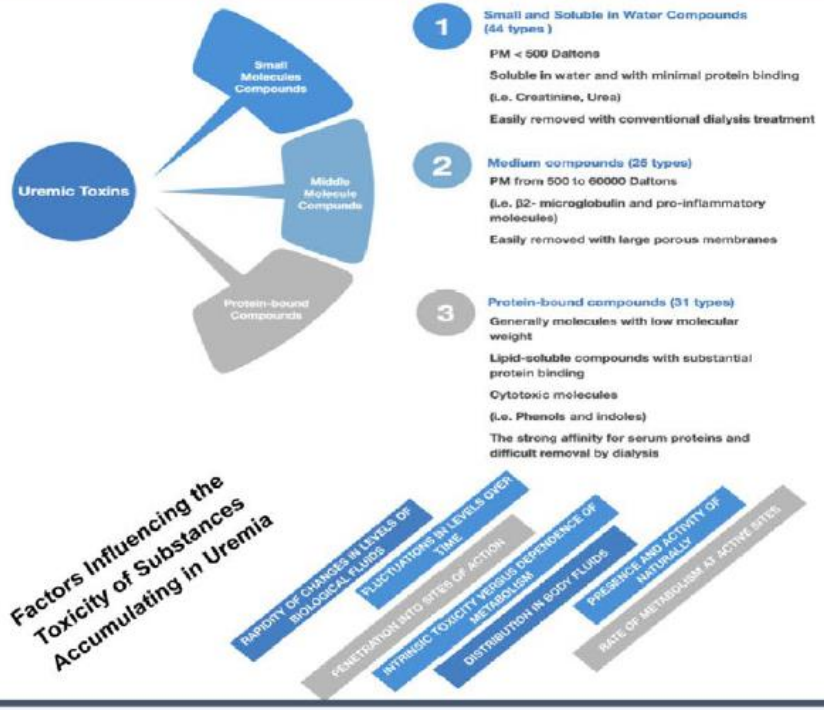
3 Anesthesia and Intensive Care, Santa Chiara Regional Hospital, APSS Trento, Trento, Italy

Background

The accumulation of uremic toxins in patients with renal failure contributes to organ dysfunction at the cellular and molecular levels. Recent dialytic approaches using medium cut-off membranes, in the context of acute kidney injury (AKI) and chronic kidney disease (CKD) patients, could lead to potential benefits in removing uremic toxins and improving patient outcomes.

Methods and Aims

The review presents the state-of-the-art on the clinical application of medium cut-off membranes in AKI and CKD patients analyzing the publications made between January 2012 and October 2023 using PubMed-indexed online databases



Conclusions

The development of medium cut-off membranes and the concept of HDx (expanded hemodialysis) represent significant progress in personalized dialysis approaches.
These membranes can effectively remove medium to high uremic toxins which are associated with disease progression, inflammation, cardiovascular risks, and mortality in both acute and chronic settings.

Journal of NEPHROLOGY
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Efficacy of medium cut-off dialyzers and comparison with high-flux dialyzers in patients on maintenance hemodialysis: A systematic review and meta-analysis

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Abstract

Medium cut-off (MCO) dialyzers were designed to provide better clearance of uremic toxins. We conducted a meta-analysis comparing MCO with high-flux (HF) dialyzers for the effect on uremic toxins in maintenance hemodialysis (HD) patients. Five databases were systematically searched for relevant studies and nine studies were identified finally. Reduction ratio (RR) of urea, urea, creatinine, β2-macroglobulin (β2-MG), kappa free light chain (κFLC), and lambda FLC (λFLC) levels were not significantly different between MCO and HF dialyzers. But RR of β2-MG, κFLC, and λFLC were greater for MCO than HF dialyzers. MCO dialyzers could better reduce tumor necrosis factor-α (TNF-α) levels. Subgroup analysis stratified by study design indicated that in randomized controlled trial (RCT) studies, albumin levels was lower in MCO than HF dialyzers group, but the two dialyzers treatments were equivalent in non-RCT subgroup. Compared with HF dialyzers, MCO dialyzers provided higher middle-molecules uremic toxins clearance and obviously reduced TNF-α levels.

KEYWORDS

albumin, hemodialysis, high-flux dialyzers, medium cut-off dialyzers, uremic toxins

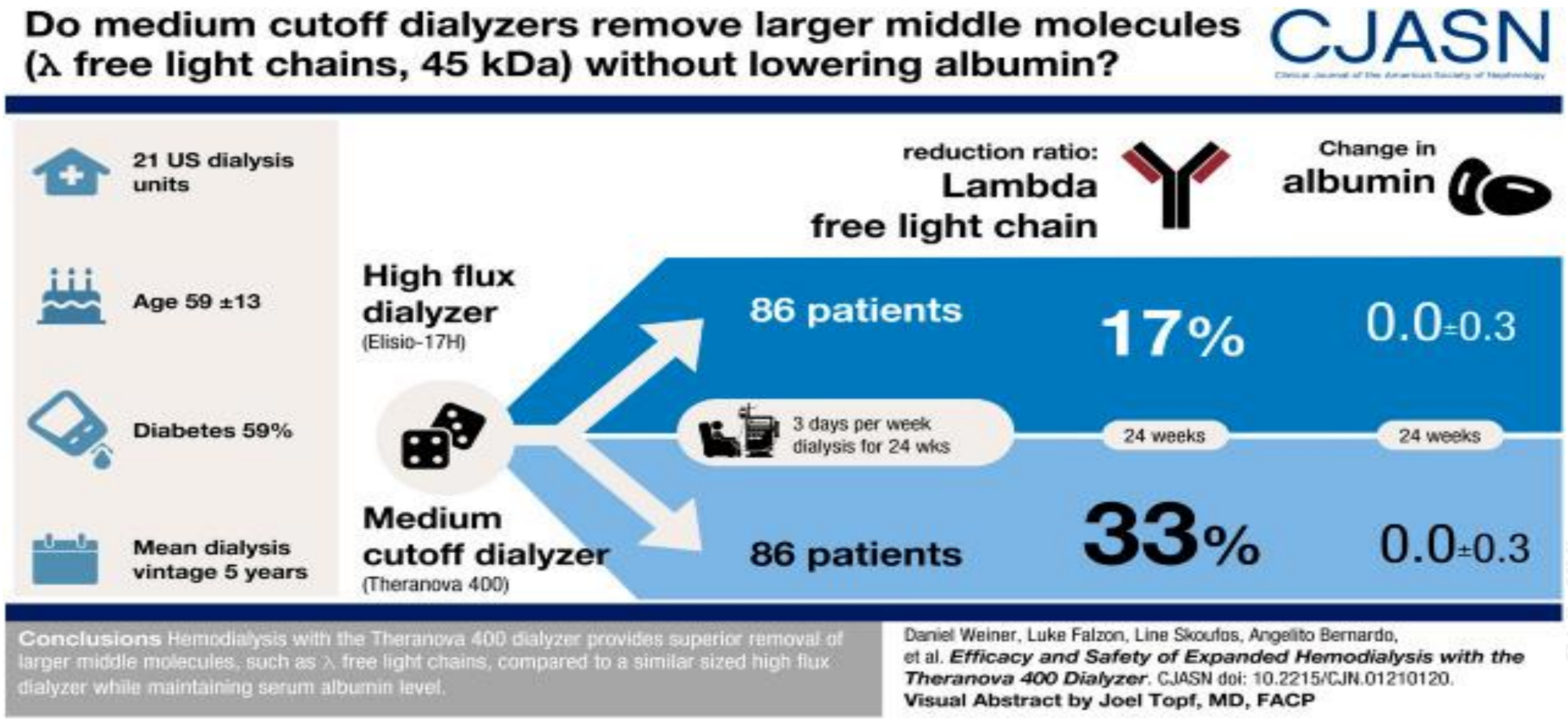
Ther Apher Dial. 2022;26:756–768.

Characteristics of included studies

Study	Region	Type of study	Number of participants	Mean age, years	Male ratio, %	Measurement time	Clinical parameters
Zickler et al. [18]	Germany	RCT	MCO: 23 HF: 25	58.9	72.9%	4 weeks of each dialysis modality + 8 weeks of extension phase	The levels of Cre, β2-MG, κFLC, λFLC, IL-6, TNF-α, albumin
Belmouaz et al. [19]	France	RCT	MCO: 20 HF: 20	75.5	70%	3 months of each dialysis modality + 3 months weeks of extension phase	The levels of urea, Cre, β2-MG, κFLC, λFLC, IL-6, TNF-α, albumin Reduction rate of urea, β2-MG, κFLC, λFLC
Sevinc et al. [20]	Turkey	RCT	MCO: 26 HF: 24	56.4	58%	12 weeks of each dialysis modality + 12 weeks of extension phase	The levels of urea, Cre, β2-MG, κFLC, λFLC, IL-6, albumin Reduction rate of urea, β2-MG, κFLC, λFLC
Lim et al. [21]	South Korea	RCT	MCO: 24 HF: 25	62.2	75%	12 weeks	The levels of BUN, Cre, β2-MG, κFLC, λFLC Reduction rate of β2-MG, κFLC, λFLC
Weiner et al. [22]	American	RCT	MCO: 86 HF: 86	59	61%	4 and 12 weeks	The levels of albumin Reduction rate of β2-MG, κFLC, λFLC
Lim et al. [23]	South Korea	RCT	MCO: 24 HF: 25	62.2	75%	12 weeks	The levels of TNF-α, albumin
Yeter et al. [24]	Turkey	Non-RCT	MCO: 15 HF: 15	52.9	66%	6 months	The levels of β2-MG, Cre, BUN, albumin Reduction rate of urea
Ahn et al. [25]	South Korea	Non-RCT	MCO: 16 HF: 18	51.6	64.7%	12 months	The levels of β2-MG, albumin Reduction rate of β2-MG
Cho et al. [26]	South Korea	Non-RCT	MCO: 38 HF: 19	54.6	57.8%	12 months	The levels of BUN, Cre, β2-MG, κFLC, λFLC, albumin Reduction rate of BUN, β2-MG, κFLC, λFLC

Concern about Serum Albumin

Efficacy and Safety of Expanded Hemodialysis with the Theranova 400 Dialyzer
A Randomized Controlled Trial



Safety Concerns :Retention of Serum Albumin

Year	First Author	Sample Size	Intervention	Time	Study Design	Pre-Dialysis Albumin Level (g/dL, Baseline vs. End)	Percentage Reduction
2017	Zickler	48	HD MCO vs. HF	12 weeks	4-week MCO 4-week HF pre-post dialysis 8-week extension	3.70 ± 0.36 3.53 ± 0.37	4.50%
2019	Belmouaz	40	HD MCO vs. HF	6 months	3-month MCO 3-month HF pre-post dialysis	3.71 ± 0.31 3.69 ± 0.43	-
2019	Cozzolino	20	HD MCO vs. HF	6 months	3-month MCO 3-month HF pre-post dialysis	3.8 (3.30–4.20) 3.6 (2.98–3.90)	5.20%
2020	Sevinc	52	HD MCO vs. HF	6 months	3-month MCO 3-month HF pre-post dialysis	3.88 (3.71–4.04) 3.62 (3.45–3.88)	6.70%
2020	Bunch	638	MCO	12 months	12 months	4.05 (4.04–4.07) 3.98 (3.96–4.00)	1.70%

Negative effect of MCO membranes on albumin removal. Researchers observed significantly decreased plasma albumin in these studies but It is noteworthy that the albumin loss that occurred with the MCO dialyzers was within the range observed in HDF treatment , which is less than transperitoneal albumin losses seen in peritoneal dialysis , and seemed to be limited compared to HCO therapy.

Effect of Expended Hemodialysis on Quality of Life (QoL)

Altogether, whether expanded hemodialysis treatment with MCO membranes can improve the QoL of patients is not clear.

Am. Soc. Nephrol. CJASN 2020, 15, 1310–1319.

Assessment of the association between increasing membrane pore size and endotoxin permeability using a novel experimental dialysis simulation set-up

Eva Schepers[1*], Griet Glorieux[1], Sunny Eloot[1], Michael Hulko[2], Adriana Boschetti-de-Fierro[2], Werner Beck[2], Bernd Krause[2] and Wim Van Biesen[1]

Abstract

Background: Membranes with increasing pore size are introduced to enhance removal of large uremic toxins with regular hemodialysis. These membranes might theoretically have higher permeability for bacterial degradation products. In this paper, permeability for bacterial degradation products of membranes of comparable composition with different pore size was investigated with a new in vitro set-up that represents clinical flow and pressure conditions.

Methods: Dialysis was simulated with an AK200 machine using a low-flux, high-flux, medium cut-off (MCO) or high cut-off (HCO) device ($n = 6$/type). A polyvinylpyrrolidone-solution (PVP) was recirculated at blood side. At dialysate side, a challenge solution containing a filtrated lysate of two water-borne bacteria (*Pseudomonas aeruginosa* and *Pelomononas saccharophila*) was infused in the dialysate flow (endotoxin ≥ 4EU/ml). Blood and dialysate flow were set at 400 and 500 ml/min for 60 min. PVP was sampled before (PVP_{pre}) and after (PVP_{post}) the experiment and dialysate after 5 and 55 min. Limulus Amebocyte Lysate (LAL) test was performed. Additionally, samples were incubated with a THP-1 cell line (24 h) and IL-1β levels were measured evaluating biological activity.

Results: The LAL-assay confirmed presence of 9.5 ± 7.4 EU/ml at dialysate side. For none of the devices the LAL activity in PVP_{pre} vs. PVP_{post} was significantly different. Although more blood side PVP solutions had a detectable amount of endotoxin using a highly sensitive LAL assay in the more open vs traditional membranes, the permeability for endotoxins of the 4 tested dialysis membranes was not significantly different but the number of repeats is small. None of the PVP solutions induced IL-1β in the THP-1 assay.

Conclusions: A realisitic in vitro dialysis was developed to assess membrane translocation of bacterial products. LAL activity on the blood side after endotoxin exposure did not change for all membranes. Also, none of the PVP_{post} solutions induced IL-1β in the THP-1 bio-assay.

Effect on mineral metabolism

› Hemodial Int. 2021 Mar 28. doi: 10.1111/hdi.12924. Online ahead of print.

Effect of a medium cut-off dialyzer on protein-bound uremic toxins and mineral metabolism markers in patients on hemodialysis

Mark K Tiong [1 2], Rathika Krishnasamy [3 4], Edward R Smith [1 2], Colin A Hutchison [5], Elizabeth G Ryan [4 6], Elaine M Pascoe [4], Carmel M Hawley [4 7 8], Tim D Hewitson [1 2], Meg J Jardine [4 9 10 11 12], Matthew A Roberts [4 13], Yeoungjee Cho [4 7], Muh Geot Wong [10 11], Anne Heath [11], Craig L Nelson [14 15 16], Shaundeep Sen [12], Peter F Mount [17], Liza A Vergara [4], Peta-Anne Paul-Brent [4], David W Johnson [4 7 8], Nigel D Toussaint [1 2]

Affiliations + expand

PMID: 33779046 DOI: 10.1111/hdi.12924

- The use of a MCO dialyzer over 24 weeks was associated with a sustained reduction in FGF23. There was no significant change in serum IS, PCS, fetuin-A, CPP-1, or CPP-2
- Further studies are required to determine whether FGF23 reduction is associated with improved patient outcomes.

Medication Costs for Erythropoietin-Stimulating Agents

Surprisingly, in a multicenter observational cohort study and a randomized controlled trial ,patients in the HDx groups showed significant decreases in intravenous iron dose, ESA dose, ERI, and medication-related estimates of cost per patient year, and significant increases in levels of serum iron and transferrin saturation (TSAT) during the follow-up period compared with those in the high-flux groups.

Nephron.2021;145(2):179-187

Therapeutic Apheresis and Dialysis2021. 25, Issue 5 p. 621-627

Cardiovascular Risk Comparison between Expanded Hemodialysis Using Theranova and Online Hemodiafiltration (CARTOON): A Multicenter Randomized Controlled Trial

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The cardiovascular and all-cause mortalities, were similar between the two groups.

The changes in cardiovascular parameters did not differ between HDx with an MCO membrane and online-HDF.

However, attention may be needed in patients with high CAC scores or scores with an increasing tendency when onlineHDF is replaced with HDx with an MCO membrane.

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JOURNAL ARTICLE

MO880
EFFECTIVENESS OF MEDIUM CUT-OFF VS HIGH FLUX DIALYZERS: A PROPENSITY SCORE MATCHING COHORT STUDY

FREE

Alejandra Molano-Triviño, Mauricio Sanabria, Jasmin Vesga, Giancarlo Buitrago, Ricardo Sánchez, Angela Rivera

1098 patients Adult Prevalent HD patients (> 90 days in HD) at Baxter Renal Care Services Colombia

follow-up until 2 year

Main cause of hospitalization was cardio-cerebrovascular

observed lower hospitalization rates in HDx group(IRR HDx/HF-HD: 0.82 95% CI 0.69 to 0.98; p=0.03)

Lower cardiovascular events rate(IRR HDx/HF-HD: 0.65 95% CI 0.47 to 0.91; p=0.01)

Pub Date: 2021-05-30 , DOI:10.1093/ndt/gfab100.005

Effects on Medication Clearance

Among the 210 study samples, vancomycin clearance was higher in the MCO group compared to high-flux the group, but it was not statistically significant.

Toxins2020, 12, 317.

High cut-off dialysis in chronic haemodialysis patients

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ABSTRACT

Background Haemodialysis patients suffer from chronic systemic inflammation and high incidence of cardiovascular disease. One cause for this may be the failure of diseased kidneys to eliminate immune mediators. Current haemodialysis treatment achieves insufficient elimination of proteins in the molecular weight range 15–45 kD. Thus, high cut-off dialysis might improve the inflammatory state.

Design In this randomized crossover trial, 43 haemodialysis patients were treated for 3 weeks with high cut-off or high-flux dialysis. Inflammatory plasma mediators, monocyte subpopulation distribution and leucocyte gene expression were quantified.

Results High cut-off dialysis supplemented by a low-flux filter did not influence the primary end-point, expression density of CD162 on monocytes. Nevertheless, treatment reduced multiple immune mediators in plasma. Such reduction proved – at least for some markers – to be a sustained effect over the interdialytic interval. Thus, for example, soluble TNF-receptor 1 concentration predialysis was reduced from median 13·3 (IQR 8·9–17·2) to 9·7 (IQR 7·5–13·2) ng/mL with high cut-off while remaining constant with high-flux treatment. The expression profile of multiple proinflammatory genes in leucocytes was significantly dampened. Treatment was well tolerated although albumin losses in high cut-off dialysis would be prohibitive against long-term use.

Conclusions The study shows for the first time that a dampening effect of high cut-off dialysis on systemic inflammation is achievable. Earlier studies had failed due to short study duration or insufficient dialysis efficacy. Removal of soluble mediators from the circulation influences cellular activation levels in leucocytes. Continued development of less albumin leaky membranes with similar cytokine elimination is justified.

Keywords High cut-off membrane, haemodialysis, inflammation, monocytes, multiplex immunoassay.

Eur J Clin Invest 2015; 45 (12): 1333–1340

Medium cut-off membranes in AKI

Taken together, the present evidence on the use of medium cut-off membranes in AKI is limited and mainly consists of observational studies focusing on the clearance of middle molecules, most of them not powered to assess association with clinical outcomes.

In addition, AKI patients are extremely heterogeneous; further work is required to better assess the role of such membranes in clinical practice

Middle cut-off membranes in the context of AKI

Effects of Medium Cutoff Membranes on Pro-Inflammatory Cytokine and Oxidative Marker Levels in Patients with Sepsis Who Developed Acute Kidney Injury

Subject Area: Nephrology

Mustafa Comoglu ; Fatih Dede; Ezgi Coskun Yenigun ; Canan Topcuoglu; Osman Inan; Enes Seyda Sahiner; Ihsan Ates

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https://doi.org/10.1159/000519881 Article history

MCO membrane was superior to HF membrane in the removal of cytokines in septic patients with AKI.

A similar effect was not observed for oxidative stress markers.

Blood Purification

Hemodialysis – Research Article

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Effect of Expanded Hemodialysis with Theranova® in Patients with COVID-19

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HDx appears to provide better clearance for TNFα and β2 microglobulin during HD session and associates lower mortality.

They propose the HDx technique for COVID-19 patients with RRT requirements since it seems to be safe and more effective than OL-HDF

Blood Purification

Critical Care Nephrology – Research Article

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Extracorporeal Removal of Myoglobin in Patients with Rhabdomyolysis and Acute Kidney Injury: Comparison of High and Medium Cut-Off Membrane and an Adsorber Cartridge

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Parameter	HCO	MCO	Adsorber	*p* value
N	13	9	6	–
Treatment duration, h	8 [6–8]	5 [4–6]	11 [10–12]	<0.001
Blood flow, mL/min	300 [300–300]	250 [250–250]	250 [250–250]	<0.001
Dialysis modality	HDF 13 (100)	HD 9 (100)	CVVHD 1 (17) HD 5 (83)	–
Pre-procedure s-myoglobin, µmol/L	65,320 [54,931–143,999]	99,379 [36,624–128,491]	53,646 [32,731–137,828]	0.82
Post-procedure s-myoglobin, µmol/L	42,849 [30,163–62,600]	47,034 [23,010–69,639]	27,583 [22,550–31,491]	0.49
Before/after comparison	$p = 0.03$	$p = 0.004$	$p = 0.06$	–
Myoglobin decrease, µmol/L	42,959 [6,539–10,6734]	56,226 [24,638–68,096]	32,554 [12,268–70,962]	0.80
Myoglobin reduction rate	0.64 [0.13–0.72]	0.54 [0.51–0.61]	0.50 [0.37–0.62]	0.83
Albumin before, g/L	31±3	27±3	28±3	0.03
Albumin after, g/L	32±3	28±33	28±5	0.03
Before/after comparison	$p = 0.56$	$p = 0.41$	$p = 0.81$	–

Data are presented as frequency (percentage), mean ± standard deviation or median [inter-quartile range]. HDF, hemodiafiltration; HD

Results from a small cohort of patients show that the MCO membrane, as a novel approach, seems to allow for efficient removal of myoglobin from the circulation, comparable to the HCO membrane

High-cutoff hemodialysis in multiple myeloma patients with acute kidney injury

As high-cutoff hemodialysis (HCO-HD) combined with chemotherapy has progressed over the last decade, questions have arisen regarding whether it can yield better clinical benefits than HFHD and other conventional hemodialysis techniques for patients with AKI caused by MM and whether there is a target threshold of serum FLC reduction in these patients.

The evidence evaluating the effectiveness of extracorporeal light chain removal in patients with AKI due to multiple myeloma is conflicting

Efficacy of high-cutoff dialysis

The efficacy of high-cutoff dialysis was evaluated in a multicenter randomized trial (MYRE) of 98 patients with newly diagnosed multiple myeloma, severe AKI requiring hemodialysis, and biopsy-confirmed light chain cast nephropathy.

At 6 and 12 months, however, rates of hemodialysis independence were higher among patients in the high-cutoff group compared with those in the conventional hemodialysis group (57 versus 35 percent at 6 months and 61 versus 38 percent at 12 months).

JAMA. 2017;318(21):2099

Groups	EuLITE (39)		MYRE (40)	
	HCO-HD	HF-HD	HCO-HD	HF-HD
Patients	43	47	46 [a]	48
Study period	2008–2013		2011–2016	
Area	UK and Germany		France	
Age (years)	66	65	68	69
Serum creatinine (μmol/L)	623	499	566	645
Previous kidney disease (%)	7	2	6 [b]	17 [b]
Serum FLCs concentration (mg/L)	κ 9,300 λ 7,200	κ 11,600 λ 7,200	6590	5230
Bone marrow plasma cells (%)	NA	NA	38	31
Albumin (g/L)	37	38	32	34
First-line chemotherapy	BAD		BD	
Follow-up (months)	24		17.5 [c]	
Hemodialysis independence rate at 3 months (%)	56	51	41	33
Myeloma response rate at 3 months (%)	NA	NA	89	63
Hemodialysis independence rate at 6 months (%)	58	66	57	35
Myeloma response rate at 6 months (%)	63	72	78	60
Hemodialysis independence rate at 12 months (%)	58	66	61	38
Myeloma response rate at 12 months (%)	42	68	NA	NA
Death rate at 12 months (%)	NA	NA	20	21
Death rate at end point (%)	37	19	28	33

NA, not available or could not obtain all of the participants' detailed information; HCO-HD, high-cutoff hemodialysis; HF-HD, high-flux hemodialysis; FLCs, free light chains; BD, bortezomib and dexamethasone; BAD, bortezomib, doxorubicin, and dexamethasone.
Age, serum creatinine, serum FLC concentration, bone marrow plasma cells, and albumin are presented as the mean or median.
Hemodialysis independence is defined as sustained renal recovery without extracorporeal techniques after treatment.
[a]Data show that 46 patients were included in the primary analysis.
[b]Data represent patients with previous kidney diseases with an estimated glomerular filtration rate greater than 30 ml/min/1.73 m^2.
[c]Data represent a median follow-up of 17.5 months (interquartile range, 12.0–30.0 months).

Protocols for HCO-HD in multiple myeloma

Hemodialysis should be performed as soon as possible when someone has indications for dialysis, such as :

- ✓ Severe acute kidney injury (AKI stage 3 [KDIGO])
- ✓ Electrolyte disorder (blood potassium elevated more than 6.5 mmol/L)
- ✓ Severe volume overload.

J Nephrol (2016) 29(6):735–46

Protocols for HCO-HD in multiple myeloma

- A session is usually conducted intermittently for durations longer than 4 h.
- A serum FLC concentration of 500 mg/L has been set as the threshold for myeloma cast nephropathy .

- Thus, most studies terminated HCO-HD when the serum FLC concentration dropped below 500 mg/L and kept using HF-HD if dialysis was still needed until the eGFR was more than 15 ml/min/1.73 m2.

- Blood and dialysate flow were set to 250–350 and 500 ml/min, respectively, with ultrafiltration performed according to clinical needs.

Loss of albumin:HCO-HD in multiple myeloma

Hutchison et al. demonstrated that HCO-HD will result in the loss of 1.5 g and 5.7 g of albumin per hour in a single HCO1100 and a series of HCO1100, and at least 12 g and 45 g of albumin will be needed for 8-h HCO-HD, respectively. (Artif Organs (2008) 32(12):910–7).

Twenty grams of albumin was frequently supplied after HCO-HD with Theralite.®.(Nefrologia (2016) 36 (4):418–26)

During HCO-HD, the loss of electrolytes, such as calcium and magnesium, is common


Thank you
for your attention