

A Randomized Trial Comparing Medium Cut-off Membrane Dialyzers with Online Hemodiafiltration for Uremic Toxins Clearance in Hemodialysis

Patients

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Supplementary materials

Supplementary Figure S1. Demonstration of reduction ratios of small-molecule, middle-molecule, and protein-bound uremic toxins compared among the online-HDF and HDx with two types of MCO dialyzers (Theranova 500® and Elisio HX21®).

Table S1. Comparison of dialysis intervention in the study sessions

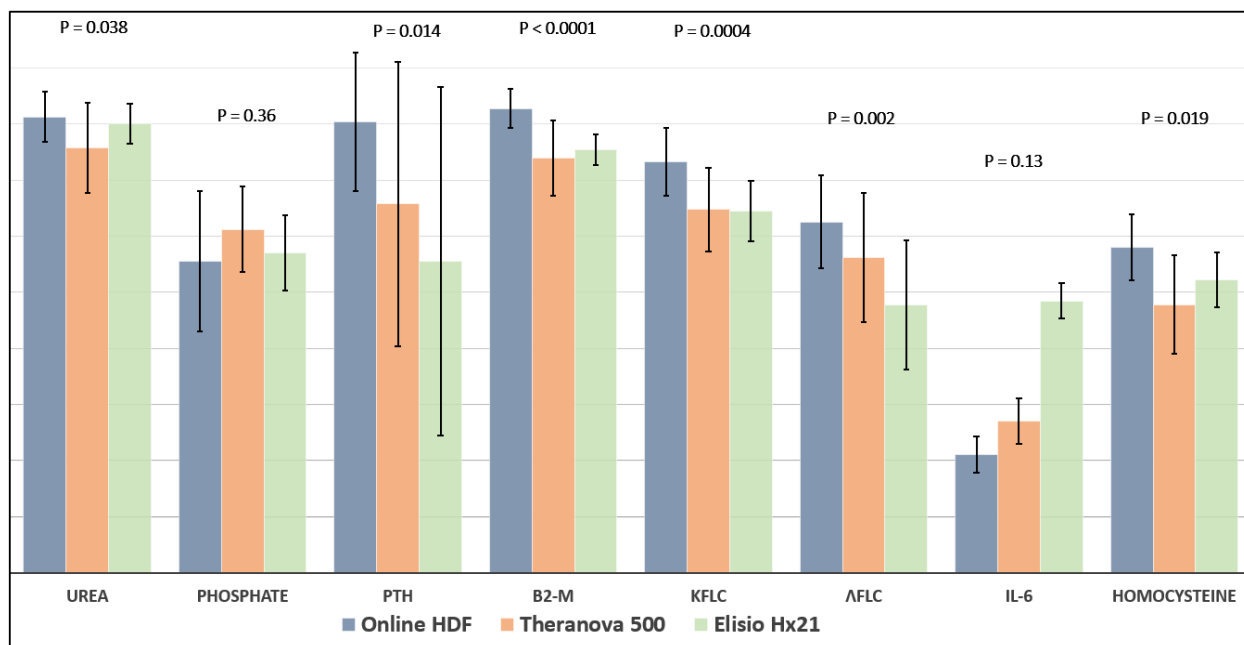
Table S2. Comparison of reduction ratios (RRs) of various uremic toxin removal between the online HDF and two types of MCO dialyzer

Table S3. Comparison of pre-dialysis uremic toxin levels at intervention initiation (week 0), week 4, and week 8 of study between the online hemodiafiltration and expanded hemodialysis with medium cut-off dialyzer groups. Values are represented as mean $\pm$ standard deviation, except the IL-6 is median (interquartile range).

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Supplementary Figure S1. Demonstration of reduction ratios of small-molecule, middle molecule, and protein-bound uremic toxins compared among the online-HDF and HDx with two types of MCO dialyzers (Theranova 500® and Elisio HX21®). PTH, parathyroid hormone; B2-M, beta-2 microglobulin; KFLC, kappa free light chain; λFLC, lambda free light chain; IL-6, interleukin-6.

Table S1. Comparison of dialysis intervention in the study sessions

	Online HDF (mean± SD)	MCO dialyzers (mean± SD)
Effective dialysis time, (min/session)	240	240
Actual blood flow rate, (mL/min)	322.5 ± 34.3	316 ± 32.7
Actual dialysis flow rate, (mL/min)	590 ± 141.0	620 ± 150.8
Actual ultrafiltration volume/session, (L)	2.4 ± 0.9	2.4 ± 1.2
Convection volume/session, (L)	24.7 ± 2.2	-
Substitution volume/session, (L)	22.2 ± 2.6	-

Online HDF, online-hemodiafiltration; MCO, medium cut-off membrane; SD, standard deviation

Table S2. Comparison of Reduction ratio (RRs) of various uremic toxin removal between the online HDF and two types of MCO dialyzer

RR of uremic toxin (%)	Online HDF (n=20)	Theranova 500® (n=10)	Elisio 21Hx® (n=10)	p-value
Urea (mean ± SD)	81.3 ± 4.5	75.7 ± 8.0	80.0 ± 3.6	0.038
Phosphate (mean ± SD)	55.5 ± 12.5	61.2 ± 7.6	57.0 ± 6.7	0.36
PTH (mean ± SD)	80.4 ± 12.3	65.7 ± 25.3	55.5 ± 31.1	0.014
β2-MG (mean ± SD)	82.8 ± 3.5	73.9 ± 6.7	75.4 ± 2.8	< 0.001
K-FLC (mean ± SD)	73.3 ± 6.0	64.7 ± 7.4	64.5 ± 5.4	< 0.001
λ-FLC (mean ± SD)	62.5 ± 8.3	56.2 ± 11.5	47.8 ± 11.5	0.002
IL-6 (mean ± SD)	21.0 ± 32.3	27.1 ± 41.1	48.5 ± 31.2	0.13
Homocysteine (mean ± SD)	58.0 ± 5.9	47.8 ± 8.8	52.2 ± 13.9	0.019

Online HDF, online hemodiafiltration; MCO, medium cut-off membrane; PTH, parathyroid hormone; β2-MG, beta-2 microglobulin; κ-FLC, kappa free light chain; λ-FLC, lambda free light chain; IL-6, interleukin-6; SD, standard deviation

Table S3. Comparison of pre-dialysis uremic toxin levels at intervention initiation (week 0), week 4, and week 8 of study between the online hemodiafiltration and expanded hemodialysis with medium cut-off dialyzer groups. Values are represented as mean $\pm$ standard deviation, except the IL-6 is median (interquartile range).

Parameters	Intervention initiation (Week 0)			Week 4			Week 8		
	OI-HDF	MCO	p-value	OI-HDF	MCO	p-value	OI-HDF	MCO	p-value
Urea (mmol/L)	19.2 $\pm$ 6.0	20.0 $\pm$ 4.0	0.60	18.9 $\pm$ 7.2	20.7 $\pm$ 4.0	0.35	18.3 $\pm$ 6.9	19.8 $\pm$ 6.8	0.50
Calcium (mg/dL)	8.6 $\pm$ 0.6	8.9 $\pm$ 0.9	0.19	8.8 $\pm$ 0.6	8.9 $\pm$ 0.8	0.59	8.7 $\pm$ 0.6	8.9 $\pm$ 0.9	0.27
Phosphate (mg/dL)	3.7 $\pm$ 1.6	4.0 $\pm$ 1.3	0.46	3.4 $\pm$ 1.5	4.1 $\pm$ 1.6	0.21	3.4 $\pm$ 1.6	4.3 $\pm$ 1.6	0.09
PTH (pg/mL)	366.1 $\pm$ 194.1	439.6 $\pm$ 285.4	0.35	289.2 $\pm$ 138.3	417.3 $\pm$ 281.5	0.08	339.4 $\pm$ 199.3	457.6 $\pm$ 310.5	0.16
CRP (mg/L)	7.4 $\pm$ 9.3	8.2 $\pm$ 9.6	0.76	9.0 $\pm$ 13.4	3.5 $\pm$ 3.1	0.08	5.4 $\pm$ 5.9	5.9 $\pm$ 8.2	0.55
β 2-MG (mg/L)	30.9 $\pm$ 10.7	32.9 $\pm$ 8.3	0.53	26.4 $\pm$ 5.5	30.0 $\pm$ 7.9	0.09	27.1 $\pm$ 4.5	30.9 $\pm$ 8.0	0.10
IL-6 (pg/mL)	8.5 (5.6 -10.5)	11.8 (8.5-24)	0.15	NA	NA	NA	5.7 (3.8-9.5)	8.7 (5.7-11.2)	0.77
K-FLC (mg/L)	251.0 $\pm$ 26.3	288.2 $\pm$ 16.8	0.19	227.1 $\pm$ 15.6	249.1 $\pm$ 18.3	0.54	196.1 $\pm$ 16.0	237.0 $\pm$ 21.6	0.13
λ -FLC (mg/L)	138.6 $\pm$ 17.5	165.8 $\pm$ 14.3	0.14	137.3 $\pm$ 7.0	144.3 $\pm$ 11.1	0.68	167.9 $\pm$ 13.5	214.9 $\pm$ 19.1	0.05
Homocysteine (U/L)	24.1 $\pm$ 5.3	23.4 $\pm$ 6.0	0.69	21.4 $\pm$ 3.8	23.2 $\pm$ 5.5	0.25	21.0 $\pm$ 3.3	21.6 $\pm$ 4.5	0.59

OI-HDF, online hemodiafiltration; MCO, medium cut-off; PTH, parathyroid hormone; CRP, C-reactive protein; β 2-MG, beta-2 microglobulin; IL-6, interleukin-6; κ -FLC, kappa free light chain; λ -FLC, lambda free light chain; NA, not applicable.

Table S4. Intradialytic complication in online HDF and MCO dialyzer groups

Intradialytic complications	Online HDF	MCO	p-value
Intradialytic hypotension			
- Event, n (%)	15 (3.1)	47 (9.8)	0.02
- Patients occurrence, n (%)	9 (45); 1-3 events*	12 (60); 1-11 events*	0.46
Intradialytic hypertension			
- Event, n (%)	28 (5.8)	12 (2.5)	0.13
- Patients occurrence, n (%)	8 (40); 1-7 events*	3 (15); 1-6 events*	0.46
Intradialytic cramping			
- Event, n (%)	6 (1.3)	6 (1.3)	1.00
- Patients occurrence, n (%)	4 (20)	5 (25)	0.74
Dialyzer clot, n (%)	4 (0.8)	1 (0.2)	0.16
Serum albumin at end study, g/dL (mean ± SD)	4.02 ± 0.24	4.00 ± 0.23	0.74

* Events/person; HDF, hemodiafiltration; MCO, medium cut-off membrane; SD, standard deviation

Table S5. Percentage change of pre-dialysis uremic toxin levels from intervention initiation to week 8

	Percentage change from initiation to week 8 (%)		
	OL-HDF	MCO	p-value
Urea (mmol/L)	-4.7 ± 16.1	-0.8 ± 26.3	0.57
Calcium (mg/dL)	1.2 ± 6.7	0.9 ± 8.8	0.88
Phosphate (mg/dL)	-3.5 ± 36.6	6.7 ± 26.3	0.32
PTH (pg/mL)	-2.5 ± 44.7	22.3 ± 70.9	0.19
CRP (mg/L)	26.5 ± 95.9	15.1 ± 191.5	0.82
β2-MG (mg/L)	-6.6 ± 23.4	-5.6 ± 16.1	0.87
IL-6 (pg/mL)	31.7 ± 150.6	-9.6 ± 94.3	0.30
K-FLC (mg/L)	-23.3 ± 15.2	-17.3 ± 18.3	0.27
λ-FLC (mg/L)	12.4 ± 35.7	29.8 ± 29.5	0.10
Homocysteine (U/L)	-9.1 ± 24.0	-4.5 ± 20.0	0.51

Online HDF, online hemodiafiltration; MCO, medium cut-off membrane; PTH, parathyroid hormone; CRP, C-reactive protein; β2-MG, beta-2 microglobulin; IL-6, interleukin-6; κ-FLC, kappa free light chain; λ-FLC, lambda free light chain; SD, standard deviation

Table S6. Dialyzer characteristics

Characteristics	Elisio 210H®	Theranova 500®	Elisio Hx21®
Membrane	Polyethersulfone (PES)	Polyarylethersulfone (PAES)	Polyethersulfone (PES)
Surface area	2.1 m ²	2.0 m ²	2.1 m ²
Priming volume	130 mL	105 mL	125 mL
Fiber inner diameter (µm)	200	180	200
Membrane thickness (µm)	40	35	40
Effective length (mm)	290	260	290
Sterilization	Dry gamma	Steam	Gamma Ray
Clearance (mL/min)*			
- Urea	291	285	292
- Creatinine	275	274	283
- Phosphate	265	267	271
Sieving coefficient			
- Vitamin B12	0.99	1.0	1.0
- Inulin	0.93	1.0	0.97
- β2-MG	0.80	1.0	1.0
- Albumin	0.002	0.008	0.0015
Sieving profile			
- MWCO (kDa)	NA	56 ± 3	NA
- MWRO (kDa)	NA	9.4 ± 0.2	NA

β2-MG, beta-2 microglobulin; MWCO, molecular weight cut-off; MWRO, molecular weight retention onset; N/A, non-available.