RENAL CARE

ELISIO™ HX

A NOVEL SHARP CUT-OFF DIALYZER

NIPRO CANADA

Live Longer. Live Better.

A novel sharp cut-off, next-generation HD dialyzer

Elisio™ HX

Chronic kidney disease (CKD) affects more than 10% of the world's population. For end stage renal disease patients, dialysis is one of the main life-sustaining treatments. However, **dialysis patients have several comorbidities and variable medical needs**.

Inflammation is at the core of the CKD leading to protein energy wasting, **anemia, malnutrition and cardiovascular (CV) diseases**.[1]

Sarcopenia, characterized by the loss of muscle mass and **frailty** also **increases CV risk and overall mortality**.[2]

With the continuous advancement in dialysis technology, a wider range of uremic toxins can be cleared in patients. High volume HDF has become the gold standard in several countries with superior survival rates.[3]

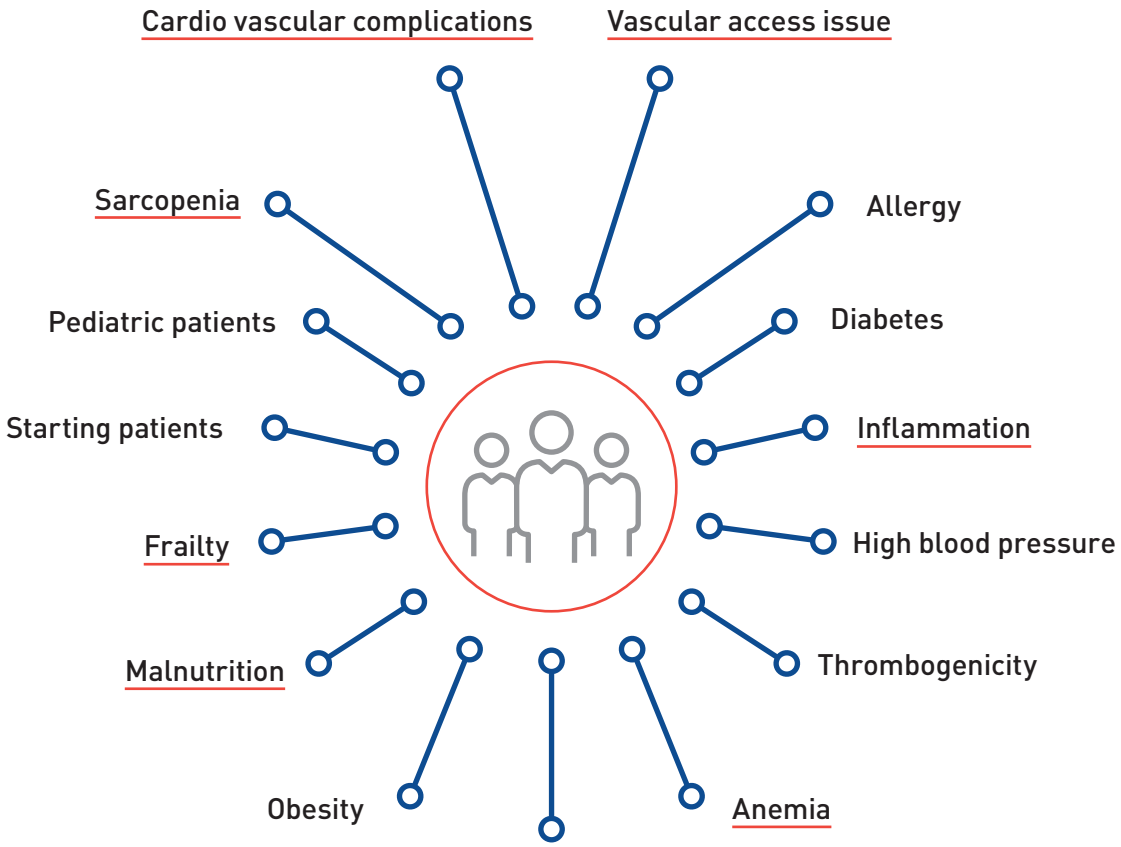
However, some patients are **not eligible for the HDF treatment** due to:

- **unsuitable vascular access**

single needle, malfunctioning central venous catheter, new fistula, low access flow not permitting the blood flow of at least 300 mL/min

- **inability to reach the efficient convective volumes (> 25 L post dilution)**[4]
- **clotting problems**
- **high hematocrit levels**

For this wide array of patients with variable medical needs, the best dialyzer should lose minimal albumin while maintaining high clearance of uremic toxins.[1]



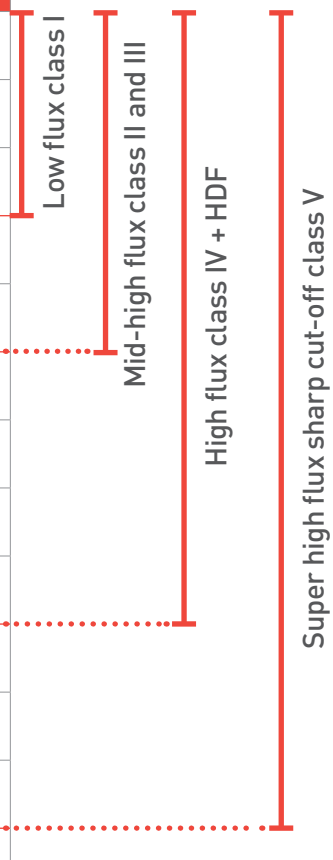
Patients with residual renal function

Nipro's novel super high flux sharp cut-off dialyzer, Elisio HX, with the combination of a bigger pore size and a specific geometry, is designed to remove a wide range of middle molecule uremic toxins (12-60 kDa) which have serious clinical impact on patients.[2]

Japanese classification of dialyzers

In the absence of HDF, conventional HD with high flux dialyzers fall short in removing **larger middle molecule uremic toxins**. To overcome this limitation, the **super high flux dialyzers** with bigger pore sizes are introduced. In Japan, this class of dialyzers – also known as high-performance membranes – are used for the treatment of more than 90% of patients on hemodialysis and are associated with **higher survival rates**.[5]

Uremic toxin	Molecular weight*
Urea	60 Da
Phosphate	96 Da
PTH	9500 Da
Beta-2 microglobulin	11.8 kDa
Myoglobin	17 kDa
Complement factor D	23.7 kDa
Interleukin-6	24.5 kDa
Kappa free light chain	25 kDa
Alpha-1 microglobulin	33 kDa
YKL-40	40 kDa
Pentraxin 3	41 kDa
Lambda free light chain	45 kDa
Albumin	67 kDa



*approximate values

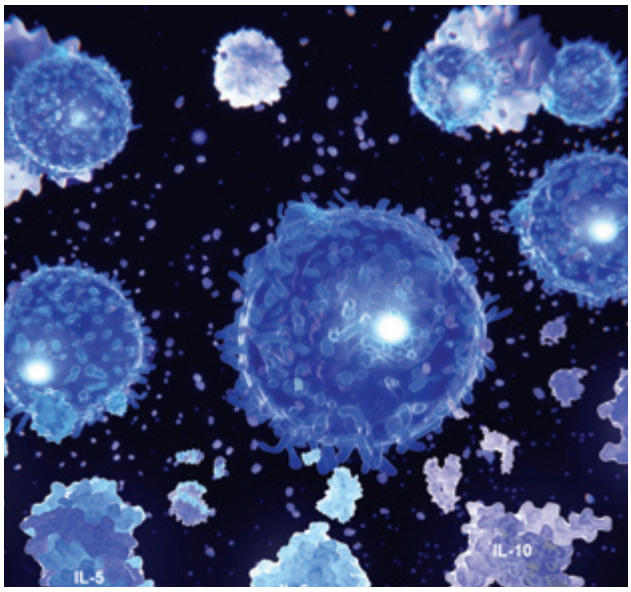
Efficacy of class V dialyzers in removing clinically impactful middle molecules

CLINICAL IMPACT OF MIDDLE MOLECULES

Inflammation

Inflammation is at the **core of the CKD pathology** leading to several complications. A **21% increase of 1st year mortality rate** has been shown **for high levels of C-reactive protein**.[6]

The RISCAVID study has demonstrated a higher **CV and all-cause mortality** risk with higher levels of **IL-6 and IL-8**.[7] **IL-18** is also linked with a higher risk of **cardio vascular mortality** in dialysis patients.[8]



Vascular calcification

An association between **serum Beta-2 microglobulin (B2M) levels and vascular calcification** has been observed suggesting the role of B2M in CV events.[9] A study with a follow-up of 6 years demonstrated this molecule as an independent predictor of **all-cause mortality**.[10]

Classically, the elevated B2M can deposit in the form of protein fibrils in various places in patients known as the **dialysis-related amyloidosis**. The effect of accumulated modified B2M is the stimulation of inflammatory molecules in the surrounding tissue leading to **tendonitis, back and neck pain** in patients.[11]

Maladaptive immunity

Plasma levels of free light chains (FLCs) increase as a result of their diminished removal in CKD patients or their excess production in diseases such as multiple myeloma.[12] The increased serum levels of FLC can interfere with the apoptosis of leukocytes leading to **increased inflammation**.[13] The **free kappa and lambda light chains** are associated with **vascular calcification**, and a higher level of the light chains may be a risk factor for **increased mortality** in CKD patients.[14-15]

Oxidative stress

In CKD, chronic inflammation, oxidative stress, and accumulation of the uremic toxins lead to the accumulation of the **advanced glycation end products (AGEs)** which can in turn aggravate the **oxidative stress and inflammation**. This vicious circle can lead to decreased muscle mass and the advancement of sarcopenia.[2]

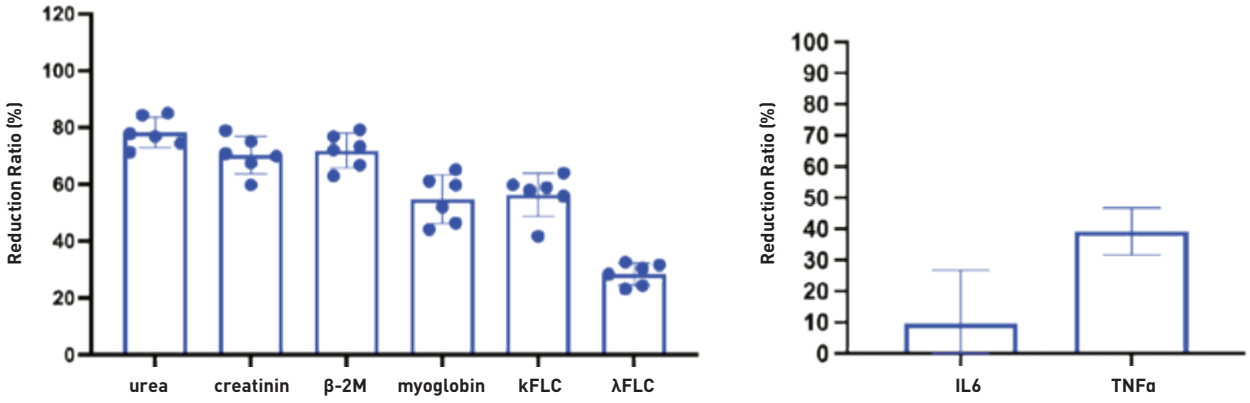
Dialysis quality dose

The glycoprotein YKL-40, an inflammatory mediator, is a significant predictor of all-cause and CV mortality in dialysis patients.[16]

The **lower serum YKL-40 concentration is associated with the higher dose (Kt/V) in dialysis**.[17] The use of the high convective volumes in this study to increase the efficiency of dialysis highlights that the **removal of middle molecules requires a higher dialysis efficacy**.

Optimal removal of middle molecule uremic toxins by Elisio HX

The objective of this prospective, single-center study was to determine the performance of the Elisio HX dialyzer in the removal of the following uremic toxins in 6 maintenance hemodialysis patients:[18]



Blood flow rate: 300 mL/min ; Dialysate flow rate: 500 mL/min; Treatment time: 240 min; N=6. Blood was collected pre- and post-dialysis to measure the reduction ratios.

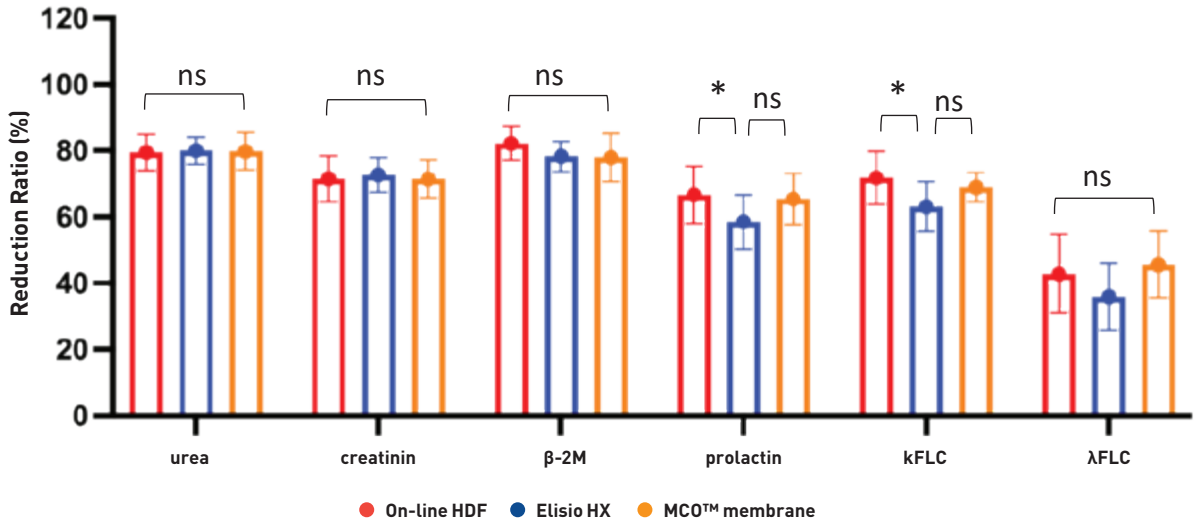
Removal of high middle molecule uremic toxins:

- reduces inflammation and oxidative stress
- improves immune response
- improves cardiovascular co-morbidities
- improves quality of life

Similar to hemodiafiltration and the medium cut-off membrane

This prospective, randomized, cross-over, single-center study was performed to determine the safety and efficacy of Elisio HX in comparison to a medium cut-off membrane and on-line HDF. 14 patients receiving HDF as baseline treatment were randomized to either Elisio HX or the the medium cut-off membrane for 1 week. The results demonstrate that the removal of the middle molecules was mainly similar between Elisio HX and the medium cut-off as well as between Elisio HX and on-line HDF.[19]

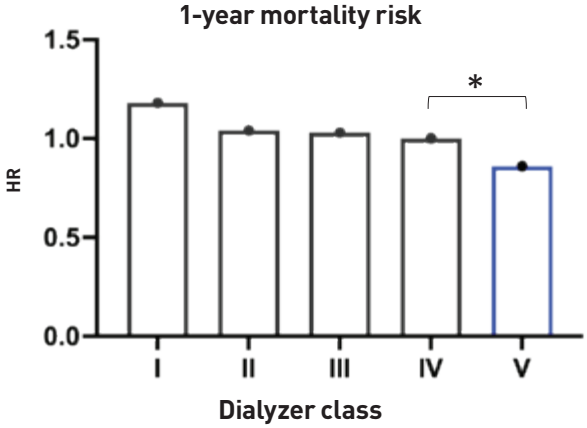
This study indicates that the treatment with Elisio HX is an suitable alternative to on-line HDF and can be utilized for patients for whom HDF treatment is not possible.



N=14; blood flow > 370 mL/min; replacement volume > 21 L; *p< 0.05; ns: not significant

Higher dialyzer performance, higher survival

Japan has been using a distinct 5-grade classification of the dialyzers based on the clearance of B2M at the blood and dialysate flow of 200 and 500 mL/min respectively. Based on this classification, **class IV and V**, also known as **super high flux** dialyzers, are identified by B2M clearance of <70, ⩾ 70, and are used for the treatment of more than 90% of patients.



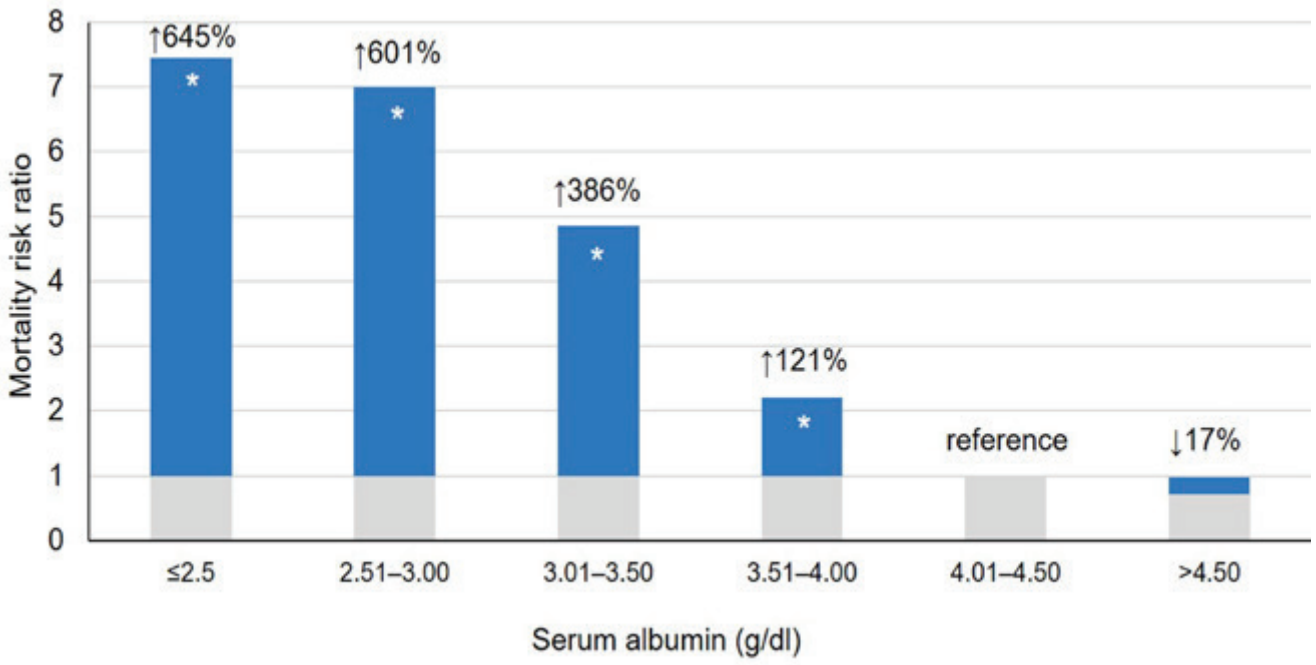
Using the nation-wide data of the Japanese society for dialysis therapy renal data registry in a large cohort of more than 200,000 patients, **this study has revealed a significantly lower risk of all-cause mortality for class V super high flux dialyzers including the sharp cut-off Elisio HX**.[5]

Graph from Abe et al.[5] 1-year all-cause mortality risk compared to class IV as reference. Cox proportional hazard regression. * p<0.05. Dialyzer classification based on B2M clearance (mL/min): I <10, II <30, III <50, IV <70, V ⩾ 70.

Minimal albumin loss in Elisio HX

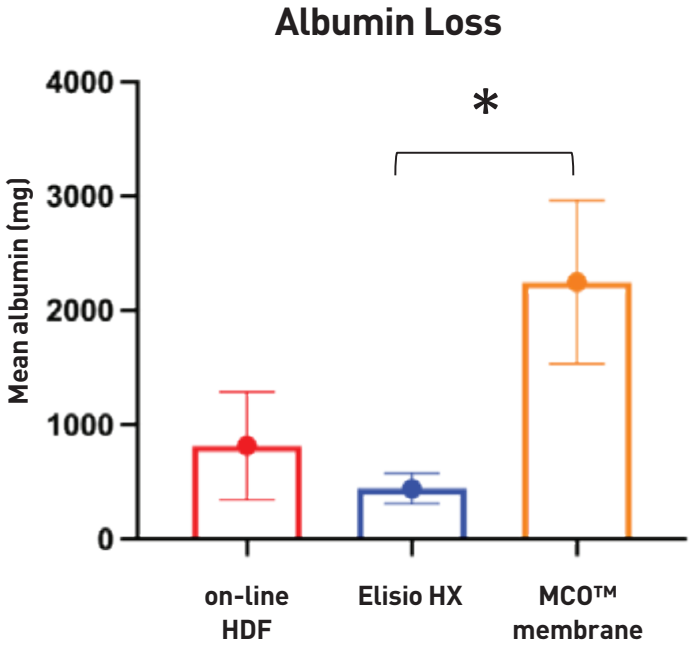
Hypoalbuminemia is common amongst the CKD patients and is a **strong predictor of mortality**.[20,21] Dialysis can increase this condition by the extra loss of albumin through the dialyzer's pores.[1]

The type of therapy and the type of membrane can impact the patients' albumin levels.[22, 23]



Graph from.[1] Relative risk of death by albumin level among 19,746 patients receiving incenter hemodialysis.[20]

The minimal albumin loss in Elisio HX, distinguishes it as a sharp cut-off membrane in the larger class of medium cut-off membranes.[19]



N=14; blood flow > 370 mL/min; replacement volume > 21 L; *p< 0.05; ns: not significant

The sharp cut-off feature of Elisio HX distinguishes this membrane for patients vulnerable to loss of albumin such as patients with malnutrition, frailty, sarcopenia or anemia.

Conclusion

Following the shift of the paradigm from one-size-fits-all to a patient-centric approach, meeting the specific needs of dialysis patients is becoming increasingly important.

HDF, as the gold standard of dialysis removes a wide array of uremic toxins associated with cardiovascular and all-cause mortality.[24] However for patients not medically eligible for HDF, the best qualitative dialysis treatment is necessary.

For patients with no access to HDF, a quality dialysis treatment should:

- remove the larger middle molecules (related to inflammation and CV diseases)[25]
- improve **amyloidosis, restless leg syndrome and pruritis**[26]
- improve the quality of life

The high performance dialyzers known as class IV and V in the Japanese classification, have shown superior survival rates and unharmful albumin losses.[5] In patients with lower capacity for albumin synthesis, or with poor nutrition, retaining sufficient **albumin is vital**.[1]

Elisio HX, with the combination of **bigger pore size and a specific geometry** is able to remove a wide range of middle molecule uremic toxins with **minimal albumin loss.** This provides a **quality dialysis treatment** for both standard and vulnerable patients.

Performance Data

Clearance: Qf = 0 mL/min*	Qb/Qd (mL/min)	11HX	13HX	15HX	17HX	19HX	21HX
Urea	200/500	191	195	197	198	199	200
	300/500	255	266	275	281	287	290
	400/500	296	313	327	338	348	355
Creatinine	200/500	179	185	190	194	197	198
	300/500	230	244	255	266	275	280
	400/500	260	280	297	310	321	331
Phosphate	200/500	173	180	186	190	194	196
	300/500	212	227	241	252	261	268
	400/500	235	253	272	286	299	310
Vitamin B_{12}	200/500	126	139	150	159	167	174
	300/500	146	163	179	192	203	214
	400/500	158	178	196	210	223	235
Myoglobin	200/500	69	80	92	102	112	121
	300/500	76	88	100	110	122	132
	400/500	81	96	108	119	130	142

Clearance Qf = 10 mL/min*	Qb/Qd (mL/min)	11HX	13HX	15HX	17HX	19HX	21HX
Urea	200/500	193	197	199	199	200	200
	300/500	257	268	276	282	288	292
	400/500	298	316	329	341	351	358
Creatinine	200/500	181	188	193	196	198	199
	300/500	233	247	258	270	277	283
	400/500	263	284	300	314	325	334
Phosphate	200/500	175	182	187	191	194	197
	300/500	216	232	245	255	264	271
	400/500	239	256	274	290	302	314
Vitamin B_{12}	200/500	129	142	153	162	170	177
	300/500	150	168	183	195	206	217
	400/500	162	182	200	214	226	240
Myoglobin	200/500	74	88	97	108	118	128
	300/500	81	94	105	116	127	139
	400/500	86	100	113	124	137	148

Ultrafiltration Coefficient

KUF (mL/hr/mmHg)	47	53	60	67	75	82

In-Vitro test conditions

Clearance: Qd 500 mL/min, Qf 0 mL/min & Qf 10 mL/min

KUF: Bovine blood (Hct 32 ±2%, Protein 60 g/L, 37°C), Qb 300 mL/min

Sieving Coefficient**

Vitamin B_{12}	1.00	β_2-microglobulin	1.00	Albumin	0.0024
Inulin	0.97	Myoglobin	0.86		

* *In vitro* test condition (EN1283, ISO 8637: 2010): Qf 0 mL/min, 10 mL/min.

Clearance data obtained in Japan. Clearance data can vary slightly depending on the test setup, lot nr. and production site.

** SC (EN1283, ISO 8637: 2010): Qb 300 mL/min, Qf 60 mL/min.

References

1. Kalantar-Zadeh K, et al. Slipping through the pores: hypoalbuminemia and albumin loss during hemodialysis. Int J Nephrol Renovasc Dis. 2021
2. Dozio E, et al. Sarcopenia in chronic kidney disease: focus on advanced glycation end products as mediators and markers of oxidative stress. Biomedicines. 2021
3. Maduell F, et al. High-efficiency postdilution online hemodiafiltration reduces all-cause mortality in hemodialysis patients. J Am Soc Nephrol. 2013
4. Maduell F, et al. ESHOL study reanalysis: All-cause mortality considered by competing risks and time-dependent covariates for renal transplantation. Nefrologia. 2016
5. Abe M, et al. High-performance dialyzers and mortality in maintenance hemodialysis patients. Sci Rep. 2021
6. Mc Causland FR, et al. C-reactive protein and risk of esrd: results from the trial to reduce cardiovascular events with aranesp therapy (treat). Am J Kidney Dis. 2016
7. Panichi V, et al. The RISCAVID study. NDT. 2008
8. Chang CH, et al. Elevation of interleukin-18 correlates with cardiovascular, cerebrovascular, and peripheral vascular events: a cohort study of hemodialysis patients. Medicine. 2015
9. Liabeuf S, et al. Plasma beta-2 microglobulin is associated with cardiovascular disease in uremic patients. KI. 2012
10. Foster MC, et al. CRIC Study. AJKD. 2016
11. Scarpioni R, et al. Dialysis-related amyloidosis: challenges and solutions. Int J Nephrol Renovasc Dis. 2016
12. Cohen G. Immune dysfunction in uremia 2020. Toxins. 2020
13. Cohen G, et al. Immunoglobulin light chains modulate polymorphonuclear leucocyte apoptosis. EJCI. 2003
14. Fraser SDS, et al. The association of serum free light chains with mortality and progression to end-stage renal disease in chronic kidney disease: systematic review and individual patient data meta-analysis. Mayo Clinic proceedings. 2017
15. Desjardins L, et al. Association between free light chain levels, and disease progression and mortality in chronic kidney disease. Toxins. 2013
16. Lorenz G, et al. Mortality prediction in stable hemodialysis patients is refined by YKL-40, a 40-kDa glycoprotein associated with inflammation. KI. 2018
17. Vega A, et al. The new marker YKL-40, a molecule related to inflammation, is associated with cardiovascular events in stable haemodialysis patients. Clin. Kidney J. 2020
18. Kreiter, et al. Internal study. 2021. Data on file
19. Puyol, et al. abstract submitted to EDTA 2022
20. Owen WF, et al. The urea reduction ratio and serum albumin concentration as predictors of mortality in patients undergoing hemodialysis. N Engl J Med. 1993
21. <https://www.dopps.org/DPM/Files/meanalbumingdl_c_overallTAB.htm. . 2020>
22. Maduell F, et al. Medium cut-off dialyzer versus eight hemodiafiltration dialyzers: comparison using a global removal score. Blood purif. 2019
23. van Gelder MK, et al. Albumin handling in different hemodialysis modalities. Nephrol Dial Transplant. 2018
24. Peters SA, et al. Haemodiafiltration and mortality in end-stage kidney disease patients: a pooled individual participant data analysis from four randomized controlled trials. NDT. 2016
25. Wolley M, et al. Exploring the clinical relevance of providing increased removal of large middle molecules. CJASN. 2018
26. Florens N, et al. Expanded haemodialysis: news from the field. NDT. 2018

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Nipro Renal Care is a global market leader with over 6 decades providing renal solutions for dialysis and dialysis-related treatment. We specialize in developing dialysis machines, water treatment systems, and a comprehensive portfolio of disposable medical equipment.

In order to address the needs of patients, healthcare professionals, and procurement managers alike, Nipro Renal Care is driven by innovation and patient safety to offer the highest quality products that optimize time, effort, and costs.

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