Chapter

Expanded Hemodialysis Therapy: From the Rational to the Delivery

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Abstract

Expanded hemodialysis therapy is a new concept in blood purification technology using a specific membrane with a steep sieving curve characterized by medium membrane cutoff and high retention onset values that are close to but lower than those of albumin. Expanded hemodialysis therapy thereby targets an important pathophysiologic link to many of the sequelae of end-stage renal disease, by improving the clearance of medium to larger-size solutes. The significant internal filtration achieved in these hemodialyzers provides a remarkable convective clearance of medium to high solutes. This therapy does not need specific software or additional complex technology, making its application possible in every setting once the quality of the dialysis fluid is guaranteed to ensure the safe conduct of the dialysis session. The present chapter reviews the rationale for expanded hemodialysis therapy, the potential benefits, and the considerations for prescription and delivery.

Keywords: expanded hemodialysis, membrane cutoff, retention onset, internal filtration, medium molecular weight solutes

1. Introduction

In 2010, more than 2 million individuals worldwide were receiving maintenance dialysis, and this number was expected to increase to 5.4 million by 2030 [1]. Despite improvements in technology and medical care, the mortality rate of patients on maintenance dialysis remains high, with 55% dying within 5 years of initiating dialysis therapy [2]. It has even been shown that the survival in maintenance dialysis patients was lower than that for patients with several types of cancer [3].

This mortality is largely related to the accumulation of uremic toxins. The existence of an interaction between uremic toxins, inflammation and/or oxidative stress, and cardiovascular mortality is well reported in the various epidemiological studies. In accordance with the European Uremic Toxins Work Group (EUTox) database, there are currently more than 153 uremic solutes listed, and that number should increase over time [4].

According to the molecular weight of these uremic toxins, they are divided into six classes, including small water-soluble molecules (<500 Da), protein-bound uremic toxins (PBUTs; mostly <500 Da), small-middle molecules (0.5–15 kDa), medium-middle molecules (15–25 kDa), large-middle molecules (25–58 kDa), and large molecules (>58 kDa) [5]. Complications, such as anemia, neuropathies, osteodystrophy,

dialysis-related amyloidosis, accelerated atherosclerosis, and cardiovascular complications, have been correlated with uremic toxins in the molecular range of 5–50 kDa [6].

Originally, membranes for hemodialysis were designed to remove small solutes, such as urea and creatinine. Since then, technological progress has continued to develop to improve the clearance of uremic toxins. The advent of ultrafiltration control systems led to the development and use of high-flux (HF) membranes that allowed improved middle molecule removal. Further evolution in technology led to the development of a new class of membranes referred to as super-flux or high cutoff (HCO), with albumin loss representing a limitation to their practical application. Hemodiafiltration (HDF) at high volumes (>23 L/1.73 m2/session) has produced some results on middle molecules and clinical outcomes, although complex hardware and high blood flows are required. A new class of membranes has recently been developed with characteristics allowing high clearances of solutes in a wide spectrum of molecular weights without significant loss of albumin. These membranes originally defined as "medium cutoff" are probably better classified as "high retention onset" and have introduced a new concept of hemodialysis called "expanded hemodialysis" (HDx). It is a simple dialysis technique, requiring no sophisticated equipment or special training for nurses, making its application possible in every setting once the quality of the dialysis fluid is guaranteed to ensure the safe conduct of the dialysis session.

In this chapter, we describe the characteristics of the medium cutoff membranes, their potential benefits, and considerations for the prescription and delivery of HDx.

2. Medium cutoff (MCO) membranes characteristics

2.1 Radius and distribution of membrane pores

Dialyzers' surface properties are crucial factors in evaluating the membrane performance. The morphological characteristics, such as mean pore size, pore size distribution, surface porosity, and pore tortuosity, influence the molecular weight removal spectrum and membrane clearance. For the MCO membrane, the size of the pores is intermediate between those of the HF and HCO membranes [7]. The MCO membrane has an effective pore radius of 3.0–3.5 nm after contact with blood, allowing for the removal of an expanded range of uremic toxins [8]. The distribution of the pores in dialysis membranes is not uniform. The more the membrane pore size distribution curves are deviated to the right, the better the removal of large middle molecules, but the risk of albumin loss is higher, it is the case with HCO membranes [9]. To improve the clearance of large middle molecules, while avoiding the loss of albumin, the distribution of the pore sizes has had to be "tightened." This is the principle used in MCO membranes.

In addition to the tight distribution of pores, there are two major differences between the MCO membrane and with HF dialyzer: first, the wall thickness is decreased from 50 μm to 35 μm, which allows a shorter diffusion path, second, the diameter of hollow fibers inside MCO membranes is reduced from the standard 200 μm to 180 μm, to improve convection and internal filtration (see internal filtration chapter below).

2.2 Sieving curves

One of the main characteristics of a dialysis membrane is its permeability in terms of sieving capacity. The sieving curve shows a progressive reduction of the observed

values for solute sieving as the solute molecular weight increases. Molecular weight cutoff (MWCO) is defined as the lowest molecular weight (in daltons) at which greater than 90% of a solute with a known molecular weight is retained by the membrane (sieving = 0.1). On the other side of the sieving curve, the molecular weight at which 10% of the solute is retained (sieving = 0.9) defines the retention onset of the membrane (MWRO). A classification scheme was proposed in which the MWCO and the MWRO are utilized in combination to define different dialyzer classes. As the separation between MWRO and MWCO decreases, the profile of the curve becomes steeper, resulting in increased removal of large uremic toxins and decreased loss of albumin [10]. Based on this concept of selectivity of the sieving coefficient, we can now differentiate the different membranes. MCO membrane, although presenting a similar MWRO to the HCO membrane, displays a completely different behavior. While MWRO for the HF membrane is in the range of 1200 Da (vitamin B12), MWRO for the MCO membrane is in the range of 12,000 Da (β-2 microglobulin). On the other side, when comparing MCO and HCO membranes, we see that these two membranes will have the same performance when extracting middle molecules, such as β-2 microglobulin, with a high MWRO for the two membranes, however, the MCO membrane has a much lower MWCO for albumin, thus making it possible to limit the leaks of albumin. For this reason, the MCO membranes have also been defined as high retention onset membranes (HRO), with the aim of optimizing clearances of medium to large MW solutes while avoiding significant albumin loss [11].

2.3 Internal filtration

Clearance of middle molecules cannot be improved by diffusive phenomena alone; convective clearance must also be optimized. Let us remember that convective clearance (K) results from the product of the UF rate (Qf) and sieving (S) of the selected molecule (K = Qf x S). Because the sieving of the selected molecule is low, the only way to increase K is to increase Qf. The on-line hemodiafiltration (OL-HDF) has made high convection rates possible thanks to the combined pre- and post-dilution configuration, but complex hardware and high blood flows are required. Due to the specific internal properties of the MCO membrane, HDx with MCO membranes represents a simpler way to improve convective clearance, with no need for fluid substitution. The ultrafiltration control system of regular hemodialysis machines provides the exact amount of net filtration required for the scheduled weight loss of dialysis patients. In OL-HDF, large amounts of ultrafiltration (UF) are achieved with high transmembrane pressure (TMP) and then replaced in the venous line after multiple steps of filtration of fresh dialysate. In HDx, the convection flow is maintained in the first part of the MCO membrane, based on excessive ultrafiltration due to the mentioned characteristics of this membrane, but it is compensated by the mechanism of internal filtration inside the filter, which takes place at about the terminal part of this membrane, and is considered as replacement fluids to the ultrafiltration [6].

The remarkable amount of convection in the proximal part is resulting from an increased end-to-end pressure drop. Internal filtration compensates for the excessive filtration rate in the distal part [12]. Thus, the convective transport of MCO membranes increases by a large margin along the length of the fibers, which makes it possible to remove large molecules with low diffusion coefficients. Indeed, to improve solute transport and avoid protein stagnation at the blood membrane interface, the diameter of hollow fibers inside MCO membranes is reduced from the standard 200 μm to 180 μm [13], which increases the rate of wall shear and blood flow velocity

[14]. Reducing the diameter and thickness of the membrane can increase internal convection by up to 30%. The combination of hydraulic permeability and geometric structure of the fibers enhances the process of internal filtration in MCO membranes [15]. MCO membranes are thus characterized by higher permeability than classic high-flux membranes. Blood flow ≥300 mL/min and dialysate flow ≥500 mL/min is sufficient to achieve optimal clearance in the system [6, 11].

3. Potential benefits of MCO membranes in HDx

3.1 Removal of ß2-microglobulin (B2M)

ß2-microglobulin is a 99 amino acid protein produced by all nucleated cells with the exception of red blood cells, it has a molecular weight of 11.8 k Daltons. It plays an important role in the immune system; it is involved in the defense against bacterial and viral infections as well as in the prevention of cancerous cells [16]. B2M accumulation in dialysis can lead to its aggregation into amyloid fibers that deposit in joint spaces causing a dialysis-related amyloidosis, resulting in carpal tunnel syndrome, arthropathy, and organ deposition of amyloid proteins [17]. It can also cause inflammation and immune dysfunction. B2M accretion has been associated with a decrease in residual kidney function [18] and an increased risk of all-cause, cardiovascular and infectious deaths [19–20]. Serum B2M remains positively associated with mortality, in a study of 23,976 patients, conducted by the Dialysis Outcomes and Practice Patterns Study (DOPPS) over a period of 10 years [17].

Convective techniques, including HDF and HF dialysis, provide better removal of middle molecules. In addition, several randomized controlled studies suggest that HF dialyzers are more effective in removing B2M than low flux membranes. Regarding HDx, studies have shown that HDx with MCO membranes results in a greater reduction ratio of a broad range of molecules, including B2M compared to HF membranes [8, 20–23]. There are several factors that can affect the clearance of B2M [8], in the study conducted by Lim [24], the reduction ratio achieved was slightly lower, and the B2M clearance was not significantly different, which was probably due to a low blood flow rate. B2M levels were found to be more important than initial levels even after one year of HDX.

Another factor that may influence the inability to remove the B2M is the rebound phenomenon, probably secondary to resistance due to a massive transfer between different body compartments that limits the clearance of B2M [25], leading sometimes to an increase in B2M levels even with MCO membranes [26].

3.2 Removal of free light chain (FLC)

Monoclonal free light chains of immunoglobulin kappa or lambda isotype have a molecular weight of 22.5 kDa and 45 kDa, respectively. They are metabolized by the kidney and can be detected in blood or urine. These FLC can polymerize in the form of dimer or multimer and thus reach high molecular weights of up to 900 kilodaltons [8]. Recently, they have been identified as toxic molecules in uremic patients [27]. Serum FLC levels have been shown to be associated with increased mortality in end-stage renal disease [27]. Therefore, FLC could be biomarkers of medium and large molecules that can be eliminated by hemodialysis, especially since their

determination is not expensive and are available in most laboratories. In patients with dialysis-dependent myeloma cast nephropathy, early FLC removal by intensive hemodialysis (IHD) with an adsorbent polymethylmethacrylate membrane (IHD-PMMA) combined with chemotherapy was associated with high rates of renal recovery and survival [28]. In a multicenter randomized trial, including 172 hemodialysis patients showed that the reduction ratio of FLC kappa and lambda was significantly higher in the HDx group using Theranova membranes compared to the use of high flux dialysis with Elisio-17H dialyzers after 6 months. This reduction was maintained in HDx until subsequent dialysis sessions [29].

3.3 Chronic inflammation

Chronic inflammation is a major and known complication during the end-stage renal disease. Among others, serum concentration of beta2-microglobulin and inflammatory mediators have been correlated with malnutrition-inflammation-atherosclerosis and formation of amyloid deposits in bone, tendons, and joints [30]. Indeed, oxidative stress results from a disequilibrium between pre-oxidative and anti-oxidative products, several molecules of high and medium molecular weight have increased levels, particularly the pro-inflammatory cytokines interleukins 1β, 6, 18, and TNF-α with prolongation of their half-life due to the uremic state. The clinical consequences are malnutrition, increased cardiovascular risk, erythropoietin resistance, and increased all-cause mortality [31].

Studies have suggested a better removal of pro-inflammatory proteins with MCO membranes and HDx. In a study conducted on patients with acute kidney injury and sepsis suspected of having high cytokine levels, the use of MCO membrane in continuous veno-venous hemodialysis (CVVHD) had a modest clearance of most cytokines and demonstrated small to no adsorptive capacity despite a decline in plasma cytokine concentrations [32] while in the randomized crossover trial of 48 hemodialysis patients, comparing MCO dialysis to HF dialysis for 12 weeks, the authors showed a considerable reduction in the expression of cytokines -RNAm of IL2 and TNFα, in circulating leucocytes when using MCO, compared to HF dialyzers. This study showed that MCO could significantly reduce inflammatory mediators in the first weeks. This difference was absent when the study was extended to 12 weeks. There was a decrease in the initial albumin concentration with stabilization thereafter [33].

In a prospective study [34], the MCO dialysis membranes had a favorable outcome on inflammation with a decrease in C-reactive protein levels when compared to low-flow dialysis and high-flux membranes, without any effect on oxidative stress markers (paraoxonase-1, ischemia-modified albumin, total Thiol, disulfide bond, and native Thiol). In addition, in Cozzolino et al. study, there was a 50% reduction in infection rate that requires admission and systemic antibiotics in patients treated with expanded hemodialysis enabled by the medium cutoff membrane [35].

3.4 Cardiovascular parameters

It is well established that cardiovascular damage is the primary cause of morbidity and mortality in end-stage renal disease. Several factors are involved or may contribute to their aggravation (increased phospho-calcium product with vascular calcification, anemia, inflammation, and oxidative stress). Uremic toxins can induce platelet activation and aggregation, leading to the development of thrombi [36].

In a clinical trial comparing the reduction of vascular smooth muscle cell calcifications *in vitro* by MCO and HF membranes, vascular calcifications were significantly reduced *in vitro* by 24% after 4 weeks and by 33% after 12 weeks in the MCO group compared to the HF group. The concentration of calcification-associated proteins (Matrix GIa, osteopontin (OPN) and growth differentiation factor 15 (GDF-15)) was higher after incubation with HF compared to MCO. This suggests that expanded hemodialysis reduces the potential for calcifications in dialysis serum *in vitro*; these results remain to be proven *in vivo* [37]. Ciceri et al. performed a prospective, controlled, cross-over study, comparing HDx and conventional hemodialysis to analyze the pro-calcifying serum of uremic patients. Uremic serum of HDx-treated patients induced less vascular smooth muscle cells (VSMC) necrosis compared with uremic serum of HD patients. However, no differences were found between dialytic treatments in the serum potential to induce apoptosis and to modulate the expression of a panel of genes involved in VSMC simil-osteoblastic differentiation [38].

Regarding the clinical impact of HDx on cardiovascular parameters, a prospective randomized controlled trial enrolled 80 patients with HDX and HDF online. The first criterion evaluated was the changes in brachial-ankle pulse wave velocity, which did not differ between the HDX group with MCO and the HDF group. Echocardiographic parameters and cardiovascular mortality were comparable in the two groups with a tendency to increase the coronary artery calcium score in HDx [36]. HDx with MCO membranes could be a good alternative when online-HDF is not available.

3.5 Removal of proteins binding to uremic toxins (PBUT)

Despite their small molecular weight, proteins bound to albumin are difficult to remove by conventional methods. Among these molecules homocysteine, which is three to four times higher in dialysis patients, can cause inflammation, endothelial lesions, and cardiovascular damage [39]. Other small molecules, such as 3-Carboxy4-methyl-5-propyl-2-furanpropionate (MPF), tryptophan and some of its metabolites, such as indoxyl sulfate (IS), 3 indol acetic acid, kynurenine, and p-cresulfate (p-CS), bind to albumin making their removal difficult. Theoretically, a decrease in albumin would allow the elimination of these PBUTs, but studies conducted to compare this clearance between HDx and conventional HD showed contradictory results regarding the elimination of these molecules [40]. A sub-study of the REMOVAL-HD trial, enlisting 89 participants, found no significant changes in total or free levels of IS or p-CS after 12 or 24 weeks of MCO membrane use compared to baseline, as no significant albumin loss was observed in this study. Whereas an open-label, controlled, cross-over study comparing HDx and conventional HD found a significant decrease in IS and other metabolites in the HDx group [38]. Further long-term, randomized studies are needed to prove whether PBUTs clearance by HDx is superior to other techniques and to evaluate its clinical impact.

3.6 Quality of life

The evaluation of health-related quality of life (QOL) in end-stage renal disease became more and more important. Patients on dialysis suffer from symptoms, such as fatigue, cramps, loss of appetite, and pruritus [41]. Those signs are mostly related to the accumulation of uremic toxins, anemia, and cardiovascular complications, which altered mental and physical health. A decrease in QOL is also associated with an increase in mortality [42].

Several studies aimed to compare the use of HDx with conventional hemodialysis or HDF in improving QOL parameters, using several scores (LEVIL, KDQOL -SF 36, PROM POS-S Renal Symptom questionnaire and the "Recovery time from last dialysis session) [43, 44]. The major items assessed were dialysis symptom index, restless legs syndrome, sleep, energy, and well-being. In a prospective multicenter observational study of the COREXH registry, 992 patients were switched from HF to HDx for one year. The results showed that the items' symptoms, effects of kidney disease, and burden of kidney disease, improved as well as restless leg syndrome, which decreased significantly over a 12-month monitoring period [45]. Multiple studies [24, 46] showed an upgrade in QOL in patients on HDx compared to HDF or conventional HD. Bolton et al., when switching from regular high-flux dialysis membrane to medium cutoff (MCO) membrane, and evaluating different symptoms burden by the POS-S Renal total symptom score, showed a decrease at 6 months. The fatigue and lack of energy improved constantly; the percentage of participants scoring its impact as "severe" decreased from 28% at baseline to 16% at 12 months [44]. Other studies using the KDQol-36 and the Edmonton symptom assessment system revised (ESAS-r), did not demonstrate any effect of HDx on QOL [29, 47]. Studies were conducted to evaluate biomarkers for the best use of the distinctive features and benefits of HDF, α 1-MG is one biomarker that could evaluate this removal performance. The authors concluded that hemodiafilter should provide an α 1-MG removal rate of 35%. An improvement in clinical manifestations can be expected by doing so, and it increases patients' QOL [48].

The HDx with MCO membranes can improve the QOL of patients. The use of this technique may be of use in the targeted selection of patients and assist in monitoring response. The study's results are encouraging and suggest the use of HDx even in patients who cannot benefit from convective techniques because of vascular access or intolerance to high volumes of exchange [49].

3.7 Safety concerns

3.7.1 Albumin loss

HDx allows the removal of large molecules (>45 k daltons), including albumin, due to its large pore size distribution [39]. In the studies that evaluated albumin removal by HDx, there was a controversy between those showing a significant decrease versus those where the level of albumin remained the same. Even when the decrease was significant, there were no clinical signs of hypoalbuminemia, some patients reported a better appetite after switching to the HDx therapy [29, 45]. This is probably due to better removal of leptin, obsestatin, and acyl ghrelin associated with a drop in appetite among dialysis patients [50].

In the large observational study from the COREXH registry, the observed variability from baseline and maximum average change in mean serum albumin levels were − 1.8% and − 3.5%, respectively. No adverse events were related to the MCO membrane [51].

On the other hand, a slight decrease in serum albumin might be beneficial for dialysis patients. HDx might induce a moderate removal of PBUTs, oxidized albumin, and carbamylated albumin along with the serum albumin loss [51].

3.7.2 Pyrogene retention

The larger pore sizes of MCO membranes have raised concerns about the potential for increased membrane permeability to pyrogens including endotoxins and other

bacterial contaminants that could be present in the dialysis fluid, which can contribute to the pathological features of uremia in patients receiving dialysis. Hulko et al. tested the capacity of low-fux, high-fux, MCO, and HCO dialyzer membranes with different pore sizes to prevent pyrogens crossing from dialysate to the blood side in a closed-loop test system, differentiating among lipopolysaccharides, peptidoglycans, and bacterial DNA using a toll-like receptor assay. Levels of lipopolysaccharides, peptidoglycans, and bacterial DNA in the blood-side samples were too low to identify potential differences in pyrogen permeability among the membranes [52].

In another study by Schepers et al., four dialysis membranes of comparable composition but with different pore sizes were tested for their permeability for endotoxins by exposing them during a 1 h *in vitro* dialysis session to dialysate contaminated with filtrates of two water-borne bacteria, *Pseudomonas aeruginosa* and *Pelomonas* saccharophila, at an endotoxin challenge at least four times the upper limit of endotoxin load (2 EU/ml) when using standard dialysis fluid. For the tested membranes, there was a nonsignificant difference in the number of the polyvinylpyrrolidone solutions, which contained a detectable amount of endotoxin after repetitive circulation through the dialyzer, be it close to the detection limit in the majority of cases [53].

These results suggest that MCO membranes are suitable for hemodialysis using ISO standard dialysis fluid quality [54], and retain endotoxins at a similar level as other membranes.

3.7.3 Effects on medication clearance

The question that comes to mind is whether the increased pore size in MCO membranes affects the retention of commonly used medications or coagulation factors in dialysis patients. Very few clinical studies have addressed this issue [55].

Using an *in vitro* model, removing erythropoietin, heparin, insulin, and several coagulation factors with HDx was comparable with HF and HDF therapy, suggesting that it is not necessary to change the medication dosing or anticoagulation protocols for dialysis patients receiving HDx therapy with MCO membranes. In the study published by Allawati et al., vancomycin clearance was higher in the MCO group compared to high-flux the group, but it was not statistically significant [56].

3.7.4 Routine use evaluation of MCO membranes

In the study by Florens et al., the authors evaluated the first routine use of HDx therapy in real-life conditions. Eighteen centers participated, and nurses and nephrologists answered by filling in a score regarding the use of MCO membranes. The assessment was related to packaging, priming, and rinsing of the dialyzers. Overall HDx therapy was easy to use in routine, and no adverse events were reported. However, nurses experienced some issues concerning poor de-aeration and the need for more anticoagulation. These problems could be prevented by training the medical staff [50].

4. For whom and how to make the prescription?

In view of the potential beneficial clinical effects associated with the use of HDx, most patients on chronic hemodialysis would be potential candidates for HDx treatment, especially since, to our knowledge, there is currently no specific

contraindication to the use of MCO membranes in patients on chronic hemodialysis. That said, some criteria can help us to choose the patients to start with and gain experience in HDx therapy.

As HDx would optimize the clearance of middle molecules, it would ideally be prescribed in patients who have the greatest retention of large middle molecules and those who would have the greatest benefit from increased removal of these molecules. Among these patients, mention may be made of anuric patients, since serum concentrations of middle-molecules are closely correlated with residual renal function, patients with a long-expected lifespan, without kidney transplant project, patients with persistent hyperphosphatemia, and patients with chronic inflammation, erythropoietin resistance, secondary immunodeficiency, and cardiovascular disease [30, 57]. Moreover, there are some promising applications in which HDx could have an interest: pruritus, post-HD asthenia, anorexia, restless legs syndrome, myeloma, and rhabdomyolysis [50].

Compared to the OL-HDF, the HDx would be useful when an adequate convective volume (23 L) cannot be reached (elevated hemoglobin, suboptimal blood flow...), or when the OL-HDF needs to be suspended (dialysis without anticoagulation, one needle puncture, safety reasons) [7]. HDx is a simple dialysis technique, requiring no sophisticated equipment or special training for nurses. It can be delivered with any standard hemodialysis monitor. As described above, blood flow around 300 mL/min and dialysate flow around 500 mL/min is sufficient to achieve optimal clearance, superior to HF hemodialysis and comparable to or even exceeding HDF [13]. HDx therapy requires no specific or intensified clinical monitoring. However, as with all filters with internal filtration, the quality of dialysis fluid remains a sine qua non condition to ensure the safe conduct of the dialysis session. The manufacturer recommends that the MCO membrane should not be used in convective strategies most likely due to the potential risk of significant albumin loss [30]. Thus, especially in patients who were in HDF, or when using monitors that can perform HDF, care should be taken to verify the selected treatment mode, and switch the treatment mode to hemodialysis if not.

Another factor that should probably be considered is the length of the session. In comparison to small water-soluble solutes, the clearance of middle-molecules is affected more by the inter-compartment transfer from extra to intravascular compartments during dialysis [30]. So, it would make sense that, at least in dialysis settings where time is flexible, such as home hemodialysis, MCO membranes could be used for long or more frequent dialysis treatments to increase middle-molecule removal.

5. Conclusion

Despite advances in hemodialysis-related technologies, there was no clear progress in terms of mortality benefit and clinical outcome. The ability to remove medium-high uremic toxins could provide a potential advantage. A number of dialyzers were developed over time, from low flow membranes to high flow dialyzers, the clearance of these molecules is still limited. The most recent and promising advance in the field of hemodialysis is represented by the development of medium-cutoff, high-retention-onset membranes. The combination of conventional hemodialysis and MCO membranes define expanded hemodialysis, this innovation in the field of dialysis allows diffusion and convection in a hollow fiber dialyzer. This gives it the capacity to purify

middle and large molecules without the need for large convective volumes and without a significant albumin loss. Its simple setup and application offer the possibility to use it even in patients with suboptimal vascular access or even with an indwelling catheter. Larger studies would be needed to further quantify any beneficial effects of HDx on major clinical events. Morbidity and mortality clinical studies are needed to demonstrate at least the non-inferiority of HDx over OL-HDF.

Conflict of interest

The authors declare no conflict of interest.

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