Chapter 3

Hemodiafiltration in Acute Kidney Injury

Kullaya Takkavatakarn,
Paweena Susantitaphong and Somchai Eiam-Ong

Additional information is available at the end of the chapter

http://dx.doi.org/10.5772/intechopen.79563

Abstract

Acute kidney injury (AKI) is one of the most important complications during hospitalization, especially in critically ill patients. Recent data demonstrated that certain biomarkers including pro-inflammatory cytokines are associated with high morbidity and mortality. These biomarkers, most of which have middle molecular weight, and protein-bound uremic toxins are limitedly removed by diffusion mechanism in conventional hemodialysis. Hemodiafiltration (HDF), a new modality that combines convective clearance with diffusion, could effectively enhance removal of middle molecule and protein-bound solutes. Therefore, HDF is increasingly used in several AKI settings such as septic AKI, rhabdomyolysis-associated AKI, myeloma cast nephropathy, and contrast-induced AKI. This chapter summarizes the available HDF techniques including intermittent and continuous modes, and clinical data comprise the benefits of HDF on biomarkers and renal as well as cardiovascular outcomes. Additionally, the topic provides the proposed future directions of HDF in various AKI settings.

Keywords: acute kidney injury, hemodiafiltration, convection, diffusion, sepsis, rhabdomyolysis, myeloma

1. Background

Acute kidney injury (AKI) is one of the most serious complications of patients during hospitalization especially in critically ill patients [1]. The annual incidence and mortality of AKI have been escalating despite much improvement of patient cares [2]. Besides correcting the underlying causes of AKI, there is no specific medication for effective treatment of AKI. Nowadays, the main treatment of AKI is still limited to supportive management. However, some patients had refractory volume overload and severe metabolic derangement;

therefore, renal replacement therapy (RRT) has become a key management in patients with AKI and multi-organ failure in order to normalize fluid, electrolyte, and acid–base status. Hemodiafiltration (HDF), one of the recently innovative RRT modalities, could provide benefits in decreasing inflammatory markers and cytokines, which play an important role in various AKI entities.

2. Principles of renal replacement therapy (RRT)

There are two main transportation processes of solutes and fluid across a membrane during RRT, diffusion and convection [3].

2.1. Diffusion

Diffusion is the process of spontaneous migration of solutes from a higher concentration to a lower concentration across the semipermeable membrane until the concentration becomes equal throughout a space (**Figure 1**). Factors affecting diffusion are concentration gradients, molecular size and charge of the solutes, surface area, thickness, and solute permeability of the membrane. Diffusion is the main determinant mechanism of small solute clearance in hemodialysis (HD).

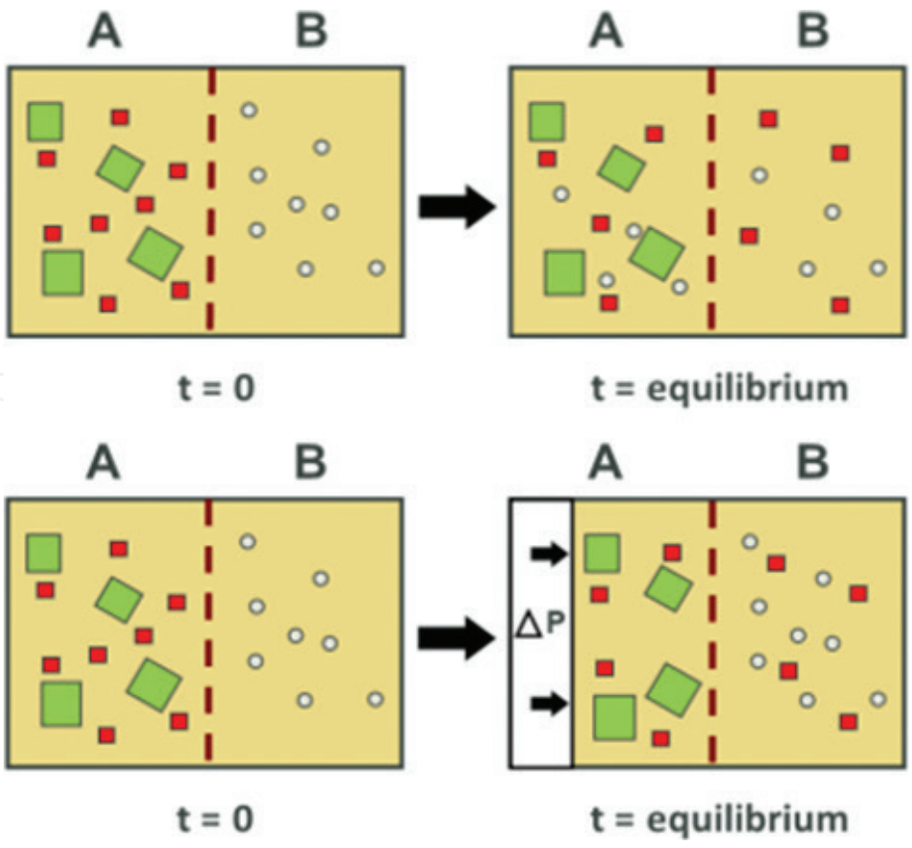

Figure 1. The processes of diffusion (top) and convection (bottom): ○ = Small solutes; ■ = Middle molecule and protein-bound solutes; ■ = Large solutes.

2.2. Convection (solvent drag)

Convection is the transportation process which the solutes migrate along with water flow (solvent) across the semipermeable membrane (**Figure 1**). Water flow or ultrafiltration is the movement of fluid across the membrane produced by transmembrane pressure gradients. There are many factors affecting the convection such as solute concentration gradients, sieving coefficient, surface area, pore size, and the permeability of membrane, but the most important one is ultrafiltration rate. Convection is able to remove protein-bound uremic toxins and middle molecule solutes such as interleukins, complement, platelet-activating factors, and other cytokines. This process is the main determinant mechanism of solute clearance in hemofiltration (HF).

3. HDF techniques

HDF is an RRT modality which combines diffusion and convection techniques to enhance the removal of middle molecule solutes and protein-bound uremic toxins by using high-flux dialyzer [4]. Therefore, this technique requires not only dialysate fluid but also sterile substitution fluid for replacement. There are various types of dilutional methods according to the site of replacement fluid infusion pre-dilution, post-dilution, mid-dilution, and mixed-dilution.

3.1. Pre-dilution HDF

In pre-dilution HDF, the replacement fluid is infused before the dialyzer (**Figure 2A**). Pre-dilution infusion reduces hemoconcentration across the membrane leading to prolongation of the extracorporeal circuit duration. However, this method provides less efficiency of solute clearance by diffusion.

3.2. Post-dilution HDF

Post-dilution HDF is the most efficient solute removal method of HDF due to high concentration gradient between blood and dialysate fluid. In post-dilution method, the replacement fluid is infused downstream the dialyzer (**Figure 2B**). An important disadvantage is that the increased hemoconcentration during high ultrafiltration rates would result in clogging of the membrane pores. Occlusion of the dialyzer leads to high transmembrane pressure gradient, reducing solute clearance, and, eventually, membrane leakage or clotting in the dialyzer.

3.3. Mid-dilution HDF

The replacement fluid is infused between two high-flux dialyzers placed in series resulting in a first post-dilution hemodiafiltration stage followed by a pre-dilution hemodiafiltration stage (**Figure 2C**). This technique can combine the advantage of both pre-dilution and post-dilution. However, the high transmembrane pressure and clotting in the first part of dialyzer are the important limitation of this technique.

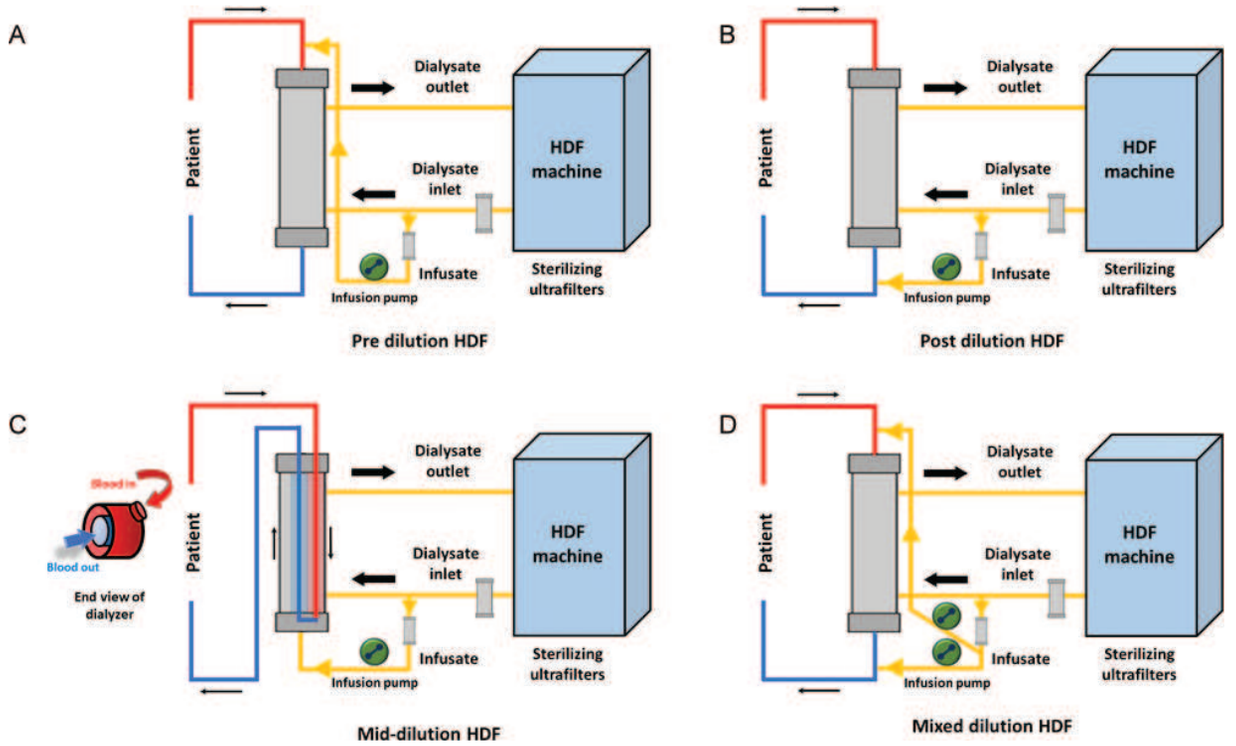

Figure 2. HDF modes according to the site of replacement fluid infusion: pre-dilution (A), post-dilution (B), mid-dilution (C), and mixed-dilution (D).

3.4. Mixed-dilution HDF

The replacement fluid is infused both before and after the dialyzer (**Figure 2D**). To reduce the unfavorable components of pre- and post-dilution HDF, the ratio of upstream and downstream infusion rates can be adjusted to achieve the optimal balance between maximizing clearance and avoiding hemoconcentration.

Of note, the efficacy of convection transport mainly depends on convection volume which consists of replacement fluid and ultrafiltration fluid. The classic HDF technique requires approximately 10 L of replacement fluid per session, while high-volume HDF uses at least 15 L per session for greater convection transport. Online HDF (OL-HDF) has been developed to reduce the high cost of commercial replacement fluid. OL-HDF is a technique using the dialysis fluid itself as the replacement fluid. After multiple steps of water purification process, the dialysis fluid becomes ultrapure before the final filtration and the last ultrafilter must have the capacity to create sterile substitutional fluid. This technique contributes a very high fluid turnover of 25–30 L per session and significantly improves middle molecule solute clearance [5, 6].

In summary, HDF has higher potency of removal of middle molecule solutes and protein-bound uremic toxins than the conventional HD [7]. Therefore, HDF would provide more benefits than conventional HD in patients with AKI particularly in certain situations, such as sepsis, rhabdomyolysis, and myeloma cast nephropathy, which requires more middle molecule solute clearance.

http://dx.doi.org/10.5772/intechopen.79563

4. HDF and sepsis-induced AKI

Sepsis is the most common cause of AKI in critically ill patients. A line of evidence shows that AKI may occur in the absence of overt hemodynamic instability. The novel concepts in the pathophysiology of sepsis-induced AKI are explained by several mechanisms, including inflammation, alteration of microcirculatory flow, and cellular responses to the inflammatory insults (**Figure 3**) [8, 9].

Firstly, the pro-inflammatory cytokines produced in sepsis such as tumor necrosis factor (TNF), interleukin-1 (IL-1), interleukin-6 (IL-6), and interferon (IFN) could contribute direct renal tubular injury [10]. In addition to the large amount of pro-inflammatory cytokines, nitric oxide and vascular endothelial growth factor (VEGF) generated during sepsis are responsible for the distortion of renal microcirculation and endothelial dysfunction [11], even with normal or increased global renal blood flow [12]. These alterations provide heterogeneity of regional blood flow distribution, impair renal autoregulation, and finally promote renal dysfunction [13, 14]. At the cellular level, mitochondria is the common target of inflammatory injury, which leads to its dysfunction, increased production of reactive oxygen species (ROS), and cell cycle arrest [15, 16].

According to these mechanisms, hemodynamic compromise does not seem to be very significant to deteriorate renal function. A previous study demonstrated that hypotension does not correlate with AKI in patients with severe sepsis [17]. Meanwhile, the production of cytokines, nitric oxide, and ROS may be the key pathogenesis of sepsis-induced AKI. Moreover, prolonged release of inflammatory mediators leads to severely impaired immunity which is followed by the secondary infection [18]. Therefore, this immunoparalysis state plays an important role in the mortality of patients with sepsis. Restoration of immune homeostasis might be able to improve the outcomes [19].

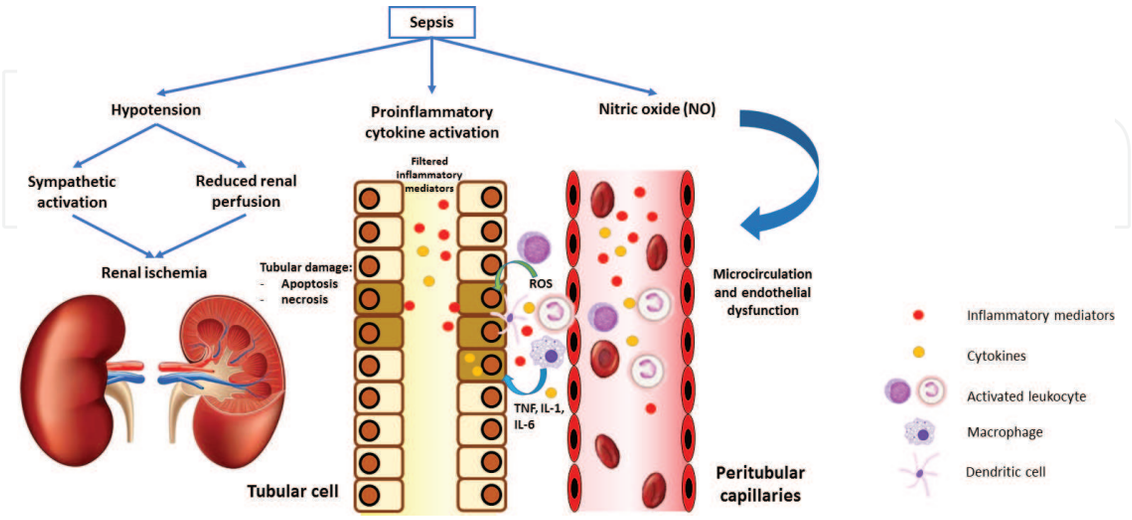

Figure 3. Pathophysiology of sepsis-induced AKI. Abbreviation: ROS, reactive oxygen species; TNF, tumor necrosis factor; IL-1, interleukin-1; IL-6, interleukin-6.

Theoretically, HDF could provide significantly higher middle molecule clearance including pro-inflammatory cytokines when compared with conventional HD. Therefore, many studies have tried to determine the benefits of HDF in sepsis-induced AKI. Indeed, a number of theories trying to explain the effects of blood purification have been proposed. First, Ronco et al. postulated that eliminating the peaks of cytokine concentration from the blood circulation during the early phase of sepsis could stop the inflammatory cascade, limit organ damage, and consequently decrease multi-organ failure [20]. The second concept is called "threshold immunomodulation hypothesis." Honore et al. proposed that cytokine removal affects not only the cytokine concentrations in bloodstream but also the level in tissues [21]. This is caused by an equilibration of their concentrations between the two compartments. According to this hypothesis, cytokines for the tissues replace those removed from the blood. Hence, no significant reduction in bloodstream cytokine concentration is observed during blood purification. The third concept is about immunomodulation. During blood purification therapy, the inflammatory cell could restore the immune function through the regulation of monocytes, neutrophils, and lymphocytes [22]. HF and HDF could play a role at this point by reducing a large amount of cytokines, terminating the inflammatory cascade, and promoting the immune recovery. However, the benefits of these modalities have been demonstrated in only limited studies.

There have been several observational studies in critically ill patients with multiple organ failure demonstrating that high-volume HF (HVHF) which prescribed at least 35 mL/kg/hr. of ultrafiltration volume or intermittent HDF improved patients' clinical outcomes [23–27]. Kron et al. performed an extended daily online high-volume HDF (6–23 hours) with convective volume about 173 L/treatment in patients with sepsis [28]. In this study, hemodynamics improved significantly during the treatment, and the 90-day survival rate compared with the survival rate predicted by severity scores (APACHE II and SAPS II) was 52 versus 19%. A previous prospective randomized controlled trial (RCT) in sepsis-induced AKI patients illustrated that pre-dilution intermittent OL-HDF for 4 hours enhanced cytokine removal over intermittent high-flux HD [29]. The clearance and reduction ratio of either pro-inflammatory or anti-inflammatory cytokines such as IL-6 (26 kDa), IL-8 (8 kDa), IL-10 (40 kDa), VEGF (46 kDa), and TNF-a (51 kDa) was significantly greater in OL-HDF than high-flux HD modality. Moreover, OL-HDF showed some better clinical outcomes including renal recovery and shorter length of hospital stay. Nevertheless, there was no significant difference in mortality between these two modalities. Another RCT, which compared every day or every alternate day of intermittent high-volume pre-dilution OL-HDF (the mean volume of replacement fluid is 81 L) to standard intermittent HD for 4 hours in critically ill ICU patients with AKI as part of multiple organ failure, failed to demonstrate the significant difference in mortality and kidney function recovery [30].

Most of critically ill patients with septic shock or hemodynamic instability require continuous RRT (CRRT). In addition to the advantage in maintaining hemodynamic stability through slow continuous ultrafiltration, many studies have proposed its ability in removal of pro-inflammatory cytokines and other middle molecule solutes through convection. Both continuous venovenous hemodiafiltration (CVVHDF) and continuous venovenous hemofiltration (CVVH) could be performed to increase convective transport. A retrospective, longitudinal follow-up study for 12 months in severe sepsis with AKI patients who received CRRT including CVVH and CVVHDF aiming at the dose of dialysis more than 35 mL/kg/hr. in ICU was performed [31]. There was no significant difference in survival rate between sepsis-induced

AKI patients treated with CVVH and CVVHDF. However, subgroup analysis in patients with oliguria/anuria showed significantly higher survival in patients treated with CVVHDF compared with CVVH. However, this result could actually be explained by the effect of residual renal clearance. In patients who still preserved diuresis, some pro-inflammatory cytokines were removed from plasma into the urine. Therefore, different CRRT modes might not affect the clinical outcomes. On the other hand, after loss of renal function, a large number of cytokines were more rapidly accumulated. A combination of diffusion and convection by CVVHDF might better control the cytokines and other uremic toxin accumulations and provided better survival outcome. However, this hypothesis needs further investigations.

4.1. Dose prescription

Besides the modalities of CRRT, the CRRT dose utilized for sepsis-induced AKI is still unestablished. Prescribed and delivered doses of CRRT in AKI vary widely. Two large, multicenter RCTs were conducted in critically ill patients with AKI to investigate the effects of RRT dose on survival benefit. The US Department of Veterans Affairs/National Institutes of Health conducted Acute Renal Failure Trial Network (ATN) study by randomly assigning 1124 critically ill patients with AKI who required RRT to high-intensity RRT (35 mL/kg/hr. of pre-dilution CVVHDF or six sessions per week of SLEDD/IHD) or low-intensity RRT (20 mL/kg/hr. of pre-dilutional CVVHDF or three sessions per week of SLEDD/IHD) [32]. The results showed survival rates after 60 days of 46% in high-intensity group and 48% in low-intensity group (p value = 0.47). In another RCT trial, the Randomized Evaluation of Normal versus Augmented Level (RENAL) of Replacement Therapy study of 1508 critically ill patients meeting the criteria for initiation RRT was included and randomly assigned to post-dilution CVVHDF with effluent rate of 40 or 25 mL/kg/hr [33]. There was no statistically significant difference of 90-day mortality between high- and low-dose RRT groups. Moreover, the secondary outcomes such as length of ICU and hospital stay, duration of mechanical ventilation therapy, and dialysis status at 90 days were not different. Both studies failed to demonstrate any benefits of using high-intensity RRT. Although the higher doses of CRRT are expected to provide more effective inflammatory cytokine removal in sepsis, subgroup analysis of patients with sepsis or organ failure revealed no significant differences in the mortality between the high- and low-intensity RRT. In addition, a recent prospective study in sepsis-induced AKI patients failed to demonstrate improvement in clinical outcomes of the high-dose pre-dilution CVVHDF over the conventional dose (80 vs. 40 mL/kg/hr) despite significant influence of high-dose CVVHDF in removal of IL-6, IL-8, and IL-10 [34]. Therefore, the KDIGO guidelines [35] proposed the optimal dose of CRRT of 20–25 mL/kg/hr in patients with AKI regardless of the etiologies of AKI. The studies examining the effects of RRT dose and outcomes are summarized in **Table 1**. However, delivering of the prescribed dose may be compromised due to filter clotting, concentration polarization of the filter, and other factors including access-related problems which diminish the treatment time. Rolando et al. studied the actual delivered dose of RRT in critically ill patients with AKI requiring dialysis. The delivered clearance was derived from the ratio of mass removal rate to blood concentration and effluent volume rate. From this study, the prescribed clearance overestimated the actual delivered clearance by 23.8% [36]. Therefore, the effluent rate prescription should be increased by 20–25% to achieve an actual prescribed dose.

Author/study	Type	Sample	Comparison/intervention	Outcomes
Comparing HDF and other modalities				
Dario et al. [23]	Multicenter, prospective, and comparative study	65 patients with AKI and sepsis	OL-HDF versus low-intensity high-flux IHD	OL-HDF showed benefits statistically significant in intensive care unit stay
Chancharoenthana et al. [29]	Single-center RCT	28 patients with AKI and sepsis	OL-HDF versus high-flux IHD	OL-HDF showed significant higher inflammatory cytokine removal, better renal recovery, and shorter length of hospital stay
Skofic et al. [30]	Single-center RCT	273 critically ill patients with AKI	High-volume OL-HDF (mean volume 81 L) versus standard IHD	No significant difference of mortality
Premuzic et al. [31]	Retrospective, longitudinal follow-up study for 12 months duration	137 patients with AKI and sepsis	CVVHDF versus CVVH aiming at the dose of dialysis >35 mL/kg/hr	No significant difference in survival rate Subgroup analysis in patients with oliguria/anuria showed significantly higher survival in patients treated with CVVHDF compared with CVVH
Effect of HDF dose and outcomes				
Kron et al. [28]	Prospective observational study	21 patients with AKI and sepsis	Extended daily online high-volume HDF (6–23 hours) with convective volume about 173 L/treatment in patients with sepsis	Significantly lower predicted mortality by APACHEII and SAPSII scores
ATN trial [32]	Multicenter RCT	1124 critically ill patients with AKI	Pre-dilution CVVHDF 35 ml/kg/r or six sessions/week of SLEDD/IHD versus pre-dilution CVVHDF 20 ml/kg/hr or three sessions/week of SLEDD/IHD	No significant difference of survival rate (46 and 48%)
RENAL trial [33]	Multicenter RCT	1508 critically ill patients with AKI	Post-dilution CVVHDF 40 ml/kg/hr versus 25 ml/kg/hr	No significant difference of survival rate (55 and 55%)
Park et al. [34]	Single-center RCT	212 patients with AKI and sepsis	High-dose pre-dilution CVVHDF 80 mL/kg/hr versus conventional dose pre-dilution CVVHDF 40 mL/kg/hr	Significant influence of high-dose CVVHDF in removal of inflammatory cytokines No significant difference of mortality

Table 1. Clinical trials using HDF in critically ill patients with AKI.

5. HDF and rhabdomyolysis-induced AKI

Myoglobin is an oxygen-binding protein found in cardiac and skeletal muscle. It has a molecular mass of 17.9 kDa. In patients with normal renal function, a rapid rise in blood myoglobin levels would be followed by a rapid disappearance within 6 hours due to high renal clearance. Myoglobin clearance decreases in renal impairment and myoglobin elimination half-life could be extended to 21 hours (range 17–29 hours) in dialyzed patients [37].

In rhabdomyolysis, myoglobin, released from injured muscle into circulation, induces renal vasoconstriction, oxidative stress, direct tubular injury, and tubular obstruction. Besides promoting urine and renal clearance of myoglobin, effective removal by extracorporeal therapies might reduce renal injuries [38]. High-flux membranes typically allow clearance of molecules up to 20 kDa, while high cutoff (HCO) membranes permit molecules with 20–50 kDa. Some larger molecules such as albumin (65 kDa) and clotting factors may also be removed when convection is applied in HCO.

There was a case series reporting on HDF with a HCO membrane applied in the treatment of acute myoglobinuric renal failure [39]. Highly efficient myoglobin removal was demonstrated. By measuring myoglobin content in the collected effluent, the single HCO-HDF for 12 hours resulted in nearly 5 grams of myoglobin removal, with a mean myoglobin clearance of 80.7 mL/min. However, a high rebound in serum myoglobin on average to 244% of the post-procedure myoglobin level was observed. Several studies also reported mass myoglobin removal on CVVHF with high-flux or HCO membranes [40–43]. However, there was no strong evidence displaying the effects of myoglobin removal on renal recovery and mortality outcome in myoglobinuric renal failure patients.

6. HDF and myeloma cast nephropathy

AKI in patients with multiple myeloma is mostly related to myeloma cast nephropathy characterized by monoclonal light chain and uromodulin obstructions in distal tubules of the kidney. Cast nephropathy is generated by massive light chain secretion in the tubules and precipitated with reduction of tubular flow. There was an RCT comparing between intensive HD (eight 5-hour sessions over 10 days) with a HCO dialyzer (HCO-HD) and conventional HD among patients who were newly diagnosed with myeloma cast nephropathy and treated with a bortezomib-based chemotherapy regimen [44]. HCO-HD allowed higher clearance of both kappa (κ) and lambda (λ) light chains. Moreover, a rapid reduction of circulating monoclonal light chains by intensive HCO-HD resulted in a statistically significant difference in HD independence at 6 and 12 months (56.5 vs. 35.4%; $p = 0.04$ and 60.9 vs. 37.5%; $p = 0.02$, respectively). However, the HD-independent rate at 3 months which was the primary outcome was not significantly different. Although using HCO membrane was likely to improve the renal outcome, higher albumin loss during HCO-HD should be considered.

Regarding HDF, there was a case series demonstrating the efficacy of supra-hemodiafiltration with endogenous reinfusion (supra-HFR) which is a subtype of HDF that utilizes separated

convection, diffusion, and adsorption [45]. The sorbent cartridge has a high affinity for both κ and λ free light chains without the drawback of albumin loss. In this report, more than 50% reduction of the serum free light chain levels occurred within only 1 week of supra-HFR treatment, and three out of four cases became dialysis independent after 2–6 weeks with no significant loss of albumin.

7. HDF and contrast-induced nephropathy (CIN)

CIN is a common cause of AKI which can range from a minor or transient elevation of serum creatinine to severe renal failure requiring dialysis. These injuries are associated with significant inhospital and long-term morbidity and mortality [46, 47]. Although various strategies in preventing CIN, such as acetylcysteine, theophylline, and other renoprotective drugs, have been evaluated, only intravenous administration of normal saline and sodium bicarbonate seem to be a useful method [48, 49].

Prophylactic HD starting immediately after administration of the contrast in patients with previous renal dysfunction failed to demonstrate the benefit in CIN prevention [50]. Nevertheless, Marenzi et al. reported the efficacy and safety of periprocedural CVVHF in chronic kidney disease patients undergoing coronary interventions (4–6 hours before coronary procedure and continued for 18–24 hours) [51]. The explanation for the discrepancy is that HD might induce hypovolemia, leading to renal hypoperfusion and renal ischemia which are important risk factors of CIN. On the contrary, CVVHF is corresponding with enhanced hemodynamic stability. In addition, CVVHF provides controlled high-volume hydration and could remove more contrast agent from the circulation, resulting in reduction of kidney exposure to the contrast agent. There was a study which compared the contrast media removing the ability of different extracorporeal treatments as low-flux HD, high-flux HD, HF, and HDF [52]. In this study, HDF and high-flux HD could effectively remove contrast media more effectively than low-flux HD and HF.

Katoh et al. performed HDF with blood suction from the right atrium (RA-HDF) in patients with renal dysfunction undergoing coronary angiography (CAG) or percutaneous coronary intervention (PCI) [53]. RA-HDF was started 30 minutes before the scheduled coronary procedure and continued until 30 minutes after the procedure. By this method, the blood was drawn from the right atrium near the orifice of the coronary sinus. Therefore, the contrast media injected into a coronary artery could be removed effectively before entering the systemic circulation. Although there was no statistically significant difference, the frequency of CI-AKI was lower in the patients receiving normal saline hydration in combination with RA-HDF compared with those administered only normal saline (12 vs. 27%). Another study investigated the use of prophylactic HDF for 3 hours after emergency or urgent CAG in acute coronary syndrome patients with severe renal (eGFR <30 mL/min/1.73 m^2) and cardiac dysfunctions (LVEF < 40%) [54]. Patients who were dialyzed with HDF had a lower incidence of severe AKI (10 vs. 40%) and lower requirement for RRT during hospitalization (7 vs. 27%). Moreover, they experienced significantly lower 1-year mortality rates than the controls. Taken together, prophylactic HDF is likely to provide salutary benefit in patients with very high risks who are undergoing coronary interventions. However, certain limitations should be

considered. First, these reports are prospective observational studies with quite small number of patients. Second, prophylactic HDF is associated with high expense, and the cost-effectiveness should be evaluated. **Table 2** details the comparison of outcomes between HDF and conventional HD in various AKI entities.

Etiology of AKI	HDF vs. conventional HD
Sepsis-induced AKI	Significantly higher cytokine removal than HD
Cytokine removal	Probable benefits
Renal recovery	No benefit
Mortality	
Rhabdomyolysis	Significantly higher myoglobin removal
	No evidence of renal recovery and mortality benefit
Myeloma cast nephropathy	Significantly higher free light chain removal
	No evidence of renal recovery and mortality benefit
Prophylaxis of contrast-induced nephropathy	Periprocedure HDF reduce incidence if CIN

Abbreviations: AKI: acute kidney injury; HDF: hemodiafiltration; HD: hemodialysis; CIN-AKI: contrast-induced nephropathy-acute kidney injury.

Table 2. Comparison of outcomes between HDF and conventional HD in various AKI settings.

8. Conclusion

By combining diffusive and convective clearances, HDF is one of the most effective modalities in clearance of middle molecule solutes and protein-bound uremic toxins. In addition to the benefit of conventional uremic toxin clearance, HDF provides a significantly higher elimination of other nephrotoxic substances. This clearance capacity seems to be associated with the improvement of renal recovery and clinical outcomes in some special entities of AKI such as sepsis, rhabdomyolysis, myeloma cast nephropathy, and CIN. However, the reduction in the mortality of patients undergoing HDF is quite difficult to be evaluated. In conclusion, while there is rising of clinical evidence favoring HDF in AKI, further large-scale prospective RCTS are essentially required to confirm its benefits.

Author details

Kullaya Takkavatakarn, Paweena Susantitaphong and Somchai Eiam-Ong*

*Address all correspondence to: somchai80754@yahoo.com

Division of Nephrology, Department of Medicine, Faculty of Medicine, Chulalongkorn University, King Chulalongkorn Memorial Hospital, Bangkok, Thailand

References

[1] Singbartl K, Kellum JA. AKI in the ICU: Definition, epidemiology, risk stratification, and outcomes. Kidney International. 2012;**81**:819-825

[2] Zeng X, McMahon GM, Brunelli SM, Bates DW, Waikar SS. Incidence, outcomes, and comparisons across definitions of AKI in hospitalized individuals. Clinical Journal of the American Society of Nephrology. 2014;**9**:12-20

[3] Denisov A. The basic principles of blood purification during hemodialysis. Terapevticheskiĭ Arkhiv. 1996;**68**:69-74

[4] Ronco C, Cruz D. Hemodiafiltration history, technology, and clinical results. Advances in Chronic Kidney Disease. 2007;**14**:231-243

[5] Tattersall JE, Ward RA, Group E. Online haemodiafiltration: Definition, dose quantification and safety revisited. Nephrology, Dialysis, Transplantation. 2013;**28**:542-550

[6] Ledebo I. On-line preparation of solutions for dialysis: Practical aspects versus safety and regulations. Journal of the American Society of Nephrology. 2002;**13**(suppl 1):S78-S83

[7] Vanholder R, Meert N, Schepers E, Glorieux G. From uremic toxin retention to removal by convection: Do we know enough? Contributions to Nephrology. 2008;**161**:125-131

[8] Gomez H, Kellum J. Sepsis-induced acute kidney injury. Current Opinion in Critical Care. 2016;**22**:546-553

[9] De Backer D, Creteur J, Preiser J, Dubois M, Vincent J. Microvascular blood flow is altered in patients with sepsis. American Journal of Respiratory and Critical Care Medicine. 2002;**166**:98-104

[10] Bonventre JV, Yang L. Cellular pathophysiology of ischemic acute kidney injury. The Journal of Clinical Investigation. 2011;**121**:4210-4221

[11] Jean-Baptiste E. Cellular mechanisms in sepsis. Journal of Intensive Care Medicine. 2007;**22**:63-72

[12] Bezemer R, Legrand M, Klijn E, Heger M, Post IC, van Gulik TM, et al. Real-time assessment of renal cortical microvascular perfusion heterogeneities using near-infrared laser speckle imaging. Optics Express. 2010;**18**:15054-15061

[13] Verma S, Molitoris B. Renal endothelial injury and microvascular dysfunction in acute kidney injury. Seminars in Nephrology. 2015;**35**:96-107

[14] Tiwari M, Brock R, Megyesi J, Kaushal G, Mayeux P. Disruption of renal peritubular blood flow in lipopolysaccharide-induced renal failure: Role of nitric oxide and caspases. American Journal of Physiology. Renal Physiology. 2005;**289**:F1324-F1332

[15] Vanhorebeek I, Gunst J, Derde S, Derese I, Boussemaere M, D'Hoore A, et al. Mitochondrial fusion, fission, and biogenesis in prolonged critically ill patients. The Journal of Clinical Endocrinology and Metabolism. 2012;**97**:E59-E64

[16] Yang QH, Liu DW, Long Y, Liu HZ, Chai WZ, Wang XT. Acute renal failure during sepsis: Potential role of cell cycle regulation. The Journal of Infection. 2009;**58**:459-464

[17] Chawla LS, Seneff MG, Nelson DR, Williams M, Levy H, Kimmel PL, et al. Elevated plasma concentrations of IL-6 and elevated APACHE II score predict acute kidney injury in patients with severe sepsis. Clinical Journal of the American Society of Nephrology. 2007;**2**:22-30

[18] Hotchkiss RS, Coopersmith CM, McDunn JE, Ferguson TA. The sepsis seesaw: Tilting toward immunosuppression. Nature Medicine. 2009;**15**:496-497

[19] Hotchkiss RS, Karl IE. The pathophysiology and treatment of sepsis. The New England Journal of Medicine. 2003;**348**:138-150

[20] Ronco C, Tetta C, Mariano F, Wratten ML, Bonello M, Bordoni V, et al. Interpreting the mechanisms of continuous renal replacement therapy in sepsis: The peak concentration hypothesis. Artificial Organs. 2003;**27**:792-801

[21] Honoré PM, Matson JR. Extracorporeal removal for sepsis: Acting at the tissue level--the beginning of a new era for this treatment modality in septic shock. Critical Care Medicine. 2004;**32**:896-897

[22] Peng Z, Singbartl K, Simon P, Rimmele T, Bishop J, Clermont G, et al. Blood purification in sepsis: A new paradigm. Contributions to Nephrology. 2010;**165**:322-328

[23] Daríoe J, Manuel G, Ana A, Miguel M, Fernando J, et al. Intermittent hemodialysis low intensity vs. on line hemodiafiltration in critically ill patients with sepsis and acute kidney injury. Choosing the best treatment in a developing country. Journal of Nephrology and Therapeutics. 2017;**7**:299

[24] Cole L, Bellomo R, Journois D, Davenport P, Baldwin I, Tipping P. High-volume haemofiltration in human septic shock. Intensive Care Medicine. 2001;**27**:978-986

[25] Cornejo R, Downey P, Castro R, Romero C, Regueira T, Vega J, et al. High-volume hemofiltration as salvage therapy in severe hyperdynamic septic shock. Intensive Care Medicine. 2006;**32**:713-722

[26] Boussekey N, Chiche A, Faure K, Devos P, Guery B, d'Escrivan T, et al. A pilot randomized study comparing high and low volume hemofiltration on vasopressor use in septic shock. Intensive Care Medicine. 2008;**34**:1646-1653

[27] Honore PM, Jamez J, Wauthier M, Lee PA, Dugernier T, Pirenne B, et al. Prospective evaluation of short-term, high-volume isovolemic hemofiltration on the hemodynamic course and outcome in patients with intractable circulatory failure resulting from septic shock. Critical Care Medicine. 2000;**28**:3581-3587

[28] Kron J, Kron S, Wenkel R, Schuhmacher HU, Thieme U, Leimbach T, et al. Extended daily on-line high-volume haemodiafiltration in septic multiple organ failure: A well-tolerated and feasible procedure. Nephrology, Dialysis, Transplantation. 2012;**27**:146-152

[29] Chancharoenthana W, Tiranathanagul K, Srisawat N, Susantitaphong P, Leelahavanichkul A, Praditpornsilpa K, et al. Enhanced vascular endothelial growth factor and inflammatory cytokine removal with online hemodiafiltration over high-flux hemodialysis in sepsis-related acute kidney injury patients. Therapeutic Apheresis and Dialysis. 2013;**17**:557-563

[30] Skofic N, Arnol M, Buturovic-Ponikvar J, Ponikvar R. Intermittent high-volume predilution on-line haemofiltration versus standard intermittent haemodialysis in critically ill patients with acute kidney injury: A prospective randomized study. Nephrology, Dialysis, Transplantation. 2012;**27**:4348-4356

[31] Premuzic V, Basic-Jukic N, Jelakovic B, Kes P. Differences in CVVH vs. CVVHDF in the management of sepsis-induced acute kidney injury in critically ill patients. Journal of Artificial Organs. 2017;**20**:326-334

[32] Network VNARFT, Palevsky PM, Zhang JH, O'Connor TZ, Chertow GM, Crowley ST, et al. Intensity of renal support in critically ill patients with acute kidney injury. The New England Journal of Medicine. 2008;**359**:7-20

[33] Investigators RRTS, Bellomo R, Cass A, Cole L, Finfer S, Gallagher M, et al. Intensity of continuous renal-replacement therapy in critically ill patients. The New England Journal of Medicine. 2009;**361**:1627-1638

[34] Park JT, Lee H, Kee YK, Park S, Oh HJ, Han SH, et al. High-dose versus conventional-dose continuous venovenous hemodiafiltration and patient and kidney survival and cytokine removal in sepsis-associated acute kidney injury: A randomized controlled trial. American Journal of Kidney Diseases. 2016;**68**:599-608

[35] Kidney disease: Improving global outcomes (KDIGO) acute kidney injury work group KDIGO clinical practice guideline for acute kidney injury. Kidney International. Supplement. 2012;**2**:1-138

[36] Claure-Del Granado R, Macedo E, Chertow GM, Soroko S, Himmelfarb J, Ikizler TA, et al. Effluent volume in continuous renal replacement therapy overestimates the delivered dose of dialysis. Clinical Journal of the American Society of Nephrology. 2011;**6**:467-475

[37] Mikkelsen TS, Toft P. Prognostic value, kinetics and effect of CVVHDF on serum of the myoglobin and creatine kinase in critically ill patients with rhabdomyolysis. Acta Anaesthesiologica Scandinavica. 2005;**49**:859-864

[38] Bosch X, Poch E, Grau JM. Rhabdomyolysis and acute kidney injury. The New England Journal of Medicine. 2009;**361**:62-72

[39] Premru V, Kovac J, Buturovic-Ponikvar J, Ponikvar R. High cut-off membrane hemodiafiltration in myoglobinuric acute renal failure: A case series. Therapeutic Apheresis and Dialysis. 2011;**15**:287-291

[40] Bastani B, Frenchie D. Significant myoglobin removal during continuous veno-venous haemofiltration using F80 membrane. Nephrology, Dialysis, Transplantation. 1997;**12**: 2035-2036

[41] Amyot SL, LeBlanc M, Thibeault Y, Geadah D, Cardinal J. Myoglobin clearance and removal during continuous venovenous hemofiltration. Intensive Care Medicine. 1999;**25**:1169-1172

[42] Hutchison CA, Harding S, Basnayake K, B radwell AR, Cockwell P. Myoglobin removal by high cut-off hemodialysis: In-vivo studies. Journal of the American Society of Nephrology. 2007;**18**:250A

[43] Naka T, Jones D, Baldwin I, Fealy N, Bates S, Goehl H, et al. Myoglobin clearance by super high-flux hemofiltration in a case of severe rhabdomyolysis: A case report. Critical Care. 2005;**9**:R90-R95

[44] Bridoux F, Carron PL, Pegourie B, Alamartine E, Augeul-Meunier K, Karras A, et al. Effect of high-cutoff hemodialysis vs conventional hemodialysis on hemodialysis independence among patients with myeloma cast nephropathy: A randomized clinical trial. Journal of the American Medical Association. 2017;**318**:2099-2110

[45] Pasquali S, Iannuzzella F, Corradini M, Mattei S, Bovino A, Stefani A, et al. A novel option for reducing free light chains in myeloma kidney: Supra-hemodiafiltration with endogenous reinfusion (HFR). Journal of Nephrology. 2015;**28**(2):251-254

[46] Weisbord S, Palevsky P. Radiocontrast-induced acute renal failure. Journal of Intensive Care Medicine. 2005;**20**:63-75

[47] Weisbord SD, Mor MK, Resnick AL, Hartwig KC, Palevsky PM, Fine MJ. Incidence and outcomes of contrast-induced AKI following computed tomography. Clinical Journal of the American Society of Nephrology. 2008;**3**:1274-1281

[48] Mueller C, Buerkle G, Buettner HJ, Petersen J, Perruchoud AP, Eriksson U, et al. Prevention of contrast media-associated nephropathy: Randomized comparison of 2 hydration regimens in 1620 patients undergoing coronary angioplasty. Archives of Internal Medicine. 2002;**162**:329-336

[49] Zhang B, Liang L, Chen W, Liang C, Zhang S. The efficacy of sodium bicarbonate in preventing contrast-induced nephropathy in patients with pre-existing renal insufficiency: A meta-analysis. BMJ Open. 2015;**5**:e006989

[50] Vogt B, Ferrari P, Schonholzer C, Marti HP, Mohaupt M, Wiederkehr M, et al. Prophylactic hemodialysis after radiocontrast media in patients with renal insufficiency is potentially harmful. The American Journal of Medicine. 2001;**111**:692-698

[51] Marenzi G, Marana I, Lauri G, Assanelli E, Grazi M, Campodonico J, et al. The prevention of radiocontrast-agent-induced nephropathy by hemofiltration. The New England Journal of Medicine. 2003;**349**:1333-1340

[52] Schindler R, Stahl C, Venz S, Ludat K, Krause W, Frei U. Removal of contrast media by different extracorporeal treatments. Nephrology, Dialysis, Transplantation. 2001;**16**:1471-1474

[53] Katoh H, Nozue T, Kimura Y, Nakata S, Iwaki T, Kawano M, et al. Elevation of urinary liver-type fatty acid-binding protein as predicting factor for occurrence of contrast-induced acute kidney injury and its reduction by hemodiafiltration with blood suction from right atrium. Heart and Vessels. 2014;**29**:191-197

[54] Marenzi G, Mazzotta G, Londrino F, Gistri R, Moltrasio M, Cabiati A, et al. Post-procedural hemodiafiltration in acute coronary syndrome patients with associated renal and cardiac dysfunction undergoing urgent and emergency coronary angiography. Catheterization and Cardiovascular Interventions. 2015;**85**:345-351

IntechOpen