Residual renal function among patients on haemodialysis and implications for clinical practice

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Abstract

The review intends to look into the benefits, impacting factors, preserving strategies especially haemodialysis (HD)-related factors and strategies as well as clinical practice implications of residual renal function (RRF) among patients on HD. Databases of Medline (Ovid), CINAHL Plus with full text (EBESCO), Embase (Ovid) and Pubmed (from January 2000 to December 2018) were searched for relevant study reports and reviews and 78 full articles were included. RRF confers a wide range of benefits for people on HD. It brings a strong survival advantage for HD populations. It provides continuous water and sodium excretion and clears middle molecular weight and protein bound uraemic toxins more efficiently. RRF also brings better management of anaemia, mineral and bone disorder, and leads to lower risk of arteriosclerosis, better nutrition and better quality of life (QOL). Intradialytic hypotension (IDH), inflammation, volume derangement, dialyser bio-incompatibility are important HD-related factors accelerating RRF decline after the initiation of HD. Studies also elucidate that incremental HD, haemodiafiltration (HDF) and peritoneal dialysis (PD) or a combination of PD and HD modality may better preserve RRF. Based on the available evidence, nephrology nurses can improve clinical practice to assist in preserving RRF among HD patients. These clinical practice implications include preventing IDH, improving dry weight assessment and volume control, advocating for incremental HD, promoting HDF, PD modality or the combination of PD and HD, improving infection control to decrease systemic inflammation, using a dialyser with further improved biocompatibility as well as promoting diuretic agents’ adherence.

Introduction

Residual renal function (RRF) in patients with end-stage kidney disease is defined as the function of remnant nephrons which includes glomerular filtration, tubular active excretion and re-absorption, renal endocrine and regulatory functions and some involvement in systemic metabolism (Lowenstein & Grantham, 2017; Shafi & Levey, 2018). After renal replacement therapy is commenced, RRF is generally considered to be the native
kidneys’ ability to excrete water, metabolic waste products and foreign substances (Roszkowska-Blaim et al., 2015). Research in the last 2 decades has demonstrated that RRF confers powerful benefits for patients on haemodialysis (HD) (Lee et al., 2017; Termorshuizen et al., 2004; Wang et al., 2018), hence preserving RRF has been recommended as one of the primary goals in managing this group of patients (Liu & Dai, 2017). Given that approximately 80% patients commence HD with some level of RRF, and the HD population comprises the majority of the dialysis population worldwide (ANZDATA, 2017; Rivara & Mehrotra, 2017; United States Renal Data System, 2018), the importance of preserving RRF for HD patients cannot be overstated. To assist nephrology nurses to better understand RRF and provide optimised care for HD patients with RRF, the review looked into RRF benefits, impacting factors, preserving strategies and nursing practice implications with an emphasis on HD-related factors and implications.

**Methodology**

The databases of Medline (Ovid), CINAHL Plus with full text (EBESCO), Embase (Ovid) and Pubmed were searched from January 2000 to December 2018. Search terms are hemodialysis/haemodialysis, hemodiafiltration/haemodiafiltration, residual renal function, residual kidney function, residual urine volume, urine volume and dialysis. Inclusion criteria are full articles of primary research reports and reviews focusing on the benefits, impacting and preserving factors of RRF among patients on HD. Exclusion criteria are studies and reviews focusing on peritoneal dialysis (PD), paediatric and acute kidney injury patients, measurement of RRF, involving non-conventional medicine, and RRF clearance of substance with unclear clinical significance. A bibliography search on the included articles was conducted. Ten primary research reports on the impact of incremental HD were removed as they had been included in the systematic review by Liu et al. (2019). A total of 78 full articles were selected on the benefit of RRF, impacting factors and preserving strategies among patients on HD.

**Benefits of RRF**

The ever-increasing research in the last 20 years has revealed that RRF confers a wide range of benefits for HD populations (Shafi et al., 2010; Termorshuizen et al., 2004; Wang et al., 2018). It confers a strong survival advantage, better fluid status, better uraemic toxin clearance, better mineral and bone disorder, lower risk of arteriosclerosis, better anaemia management, improved nutrition and better quality of life (QOL) for patients on HD. The benefits and the supporting evidence will now be explored.

**Survival benefit**

The survival benefit of RRF has been increasingly demonstrated amongst people on HD (Obi et al., 2016a; Termorshuizen et al., 2004; Wang et al., 2018). Baseline residual urine volume (RUV), as low as 100ml/day, and estimated glomerular filtration rate (eGFR) at the initiation of HD is associated with lower all-cause mortality (Lee et al., 2017; Kim & Kim, 2009; van der Wal et al., 2011). Preserved RUV and renal urea clearance (rCLurea) 1 year after the initiation of HD conferred significant survival benefit, whilst the annual declining of rCLurea and RUV had a gradient negative association with survival outcome (Mokoli et al., 2016; Obi et al., 2016a; Shafi et al., 2010). Baseline RUV was found to confer a significant survival benefit for elderly HD patients as well (Madziarska et al., 2012). rCLurea provided better protection against mortality than HD-delivered urea clearance (dCLurea) and lower dCLurea is associated with higher mortality in patients with insufficient RRF (rCLurea <3ml/min/1.73m²) only (Termorshuizen et al., 2004; Wang et al., 2018). The strong survival benefit is probably largely attributed to renal clearance of water and uraemic toxins.

**Continuous water and sodium excretion**

Renal continuous excretion of sodium and water results in better fluid status than HD intermittent fluid removal (Mathew et al., 2016). This ameliorates hypertension and left ventricular hypertrophy (LVH) directly attributed to extracellular volume overload, which precipitates cardiovascular conditions like arrhythmia, ischaemic heart disease and heart failure (Ma & Ding, 2013; Ok et al., 2017; Raikou et al., 2018). It also leads to less interdialytic weight gain (IDWG), resulting in less high ultrafiltration rate (UFR)-related intradialytic hypotension (IDH), myocardial stunning and end organ hypoperfusion (Brown et al., 2015; Chou et al., 2018; Termorshuizen et al., 2004). Thus RRF-conferring improved fluid status protects patients against hypervolaemia-related cardiovascular morbidity and high UFR-associated IDH and ischaemic organ damage.

**Clearance of middle molecular weight and protein bound uraemic toxins**

Many uraemic toxins which are poorly cleared by HD are removed via remnant nephrons (Lowenstein & Grantham, 2017; Wang et al., 2013). Plasma levels of middle molecular weight uraemic toxins like beta-2 microglobulin (β2M) and B trace protein were significantly lower in patients on maintenance HD (MHD) with RRF (Fry et al., 2007; Raikou et al., 2018; Shafi et al., 2012). Protein bound uraemic toxins like homocysteine and P-cresol sulphate were significantly lower in patients on maintenance HD with RRF (Fry et al., 2007; Raikou et al., 2018; Shafi et al., 2012). Protein bound uraemic toxins like homocysteine and P-cresol sulphate were significantly lower in patients on maintenance HD with RRF (Fry et al., 2007; Raikou et al., 2018; Shafi et al., 2012). Protein bound uraemic toxins like homocysteine and P-cresol sulphate were significantly lower in patients on maintenance HD with RRF (Fry et al., 2007; Raikou et al., 2018; Shafi et al., 2012). Protein bound uraemic toxins like homocysteine and P-cresol sulphate were significantly lower in patients on maintenance HD with RRF (Fry et al., 2007; Raikou et al., 2018; Shafi et al., 2012). Protein bound uraemic toxins like homocysteine and P-cresol sulphate were significantly lower in patients on maintenance HD with RRF (Fry et al., 2007; Raikou et al., 2018; Shafi et al., 2012). Protein bound uraemic toxins like homocysteine and P-cresol sulphate were significantly lower in patients on maintenance HD with RRF (Fry et al., 2007; Raikou et al., 2018; Shafi et al., 2012). Protein bound uraemic toxins like homocysteine and P-cresol sulphate were significantly lower in patients on maintenance HD with RRF (Fry et al., 2007; Raikou et al., 2018; Shafi et al., 2012).
molecular weight and protein bound uraemic toxins leads to reduced inflammation and pathological cardiovascular changes (Ahmadmehrai & Tang, 2018; Fry et al., 2007; Raikou et al., 2018; Shafi et al., 2012; Vanholder et al., 2018). Among the MHD patients with RRF, the levels of some vasoactive substances like catecholamine and endothelin were found to be decreased during the interdialytic period which was associated with better blood pressure (Tian et al., 2009). Both pro-inflammatory and inflammatory marker levels were found to be significantly and negatively correlated to RRF (de Seqera et al., 2017; Raikou et al., 2018; Shafi et al., 2010; Yang et al., 2009). Thus, preserved RRF leads to less inflammation and lower risk of cardiovascular morbidity.

Better management of mineral and bone disorder

RRF was associated with less metabolic disturbances and altered electrolyte status among MHD patients (Penne et al. 2011; Rhee et al., 2014; Wang et al., 2013). Serum phosphate levels were consistently found to be significantly lower in patients with renal diuresis despite significantly lower doses of phosphate binding agents (Penne et al. 2011; Rhee et al., 2014; Wang et al., 2013). Some researchers found intact parathyroid hormone (iPTH) to be significantly lower (Yang et al., 2009; Wang et al., 2013) or plasma active vitamin D3 (1,25(OH)2D3) to be significantly higher (Rhee et al., 2014) in patients with RRF. However, other researchers did not discover significant correlation between RRF and iPTH (Rhee et al., 2014), and between RRF and 1,25(OH)2D3 (Wang et al., 2013). Both rGFR and RUV were reported to be significantly correlated with urinary excretion of phosphate, and rGFR was indicated as an independent predictor of serum phosphate levels (Iwasawa et al., 2013; Wang et al., 2013). Regarding iPTH levels and mortality risk, novel findings were reported by Wang et al. (2017). Though HD patients with higher RRF consistently showed better survival, higher iPTH levels were associated with lower mortality among patients with rCLurea<1.5ml/min and with higher mortality in patients with rCLurea$\geq$1.5ml/min which was more pronounced in those with rCLurea$\geq$3.0ml/min. The authors suggested unmeasured RRF, confounding factors and patients’ non-compliance might have played a role as the association between higher alkaline phosphatase levels, another mineral and bone disorder marker, and increased mortality risk was consistent across different levels of RRF in the same cohort.

The RRF-associated more urinary phosphate excretion and lower level of serum phosphate is associated with better calcium homeostasis and less mineral and bone disorder as well as less vascular calcification.

Lower risk of arteriosclerosis

RRF has been linked to lower risk of arteriosclerosis among HD patients. RRF was found to have a strong inverse association with arteriosclerosis and serum iPTH and phosphate levels were indicated to be positively associated with arteriosclerosis (Rroji et al., 2017). Moreover, RRF (rCLurea$\geq$0.9ml/min) was reported to be significantly and negatively correlated with abdominal aortic calcification, and loss of RRF was found to be associated with vascular calcification independent of serum calcium phosphate product (Chen et al., 2016; Shin et al., 2017). Baseline RUV (<1200ml/day) was indicated as an important predictor for the risk of acute ischaemic stroke (Chen et al., 2013). The levels of fibroblast growth factor 23 (FGF-23), which are correlated to arterial stiffness and LVH, were found to have a significant and negative correlation with RRF (Iwasawa et al., 2013; Nasrallah et al., 2010; Viaene et al., 2012; Wang et al., 2013). Among HD patients, plasma levels of connective tissue growth factor, which is thought to play a role in cardiac fibrosis and artherogenesis, were reported to be significantly and negatively associated with rGFR (Gerritsen et al., 2012). The previously mentioned RRF-conferrer lower inflammatory status is thought to decrease HD patients’ susceptibility to the development and progression of arteriosclerosis (de Seqera et al., 2017; Nusair et al., 2012; Raikou et al., 2018). The negative association between RRF and the risk of arteriosclerosis indicates that RRF brings further protection against cardiovascular morbidity and mortality (Shin et al., 2017).

Better anaemia management

Whilst Louw and Chothia (2017) did not find that RUV (>100ml/ day) improved erythropoietin stimulating agent (ESA) resistance index, several other studies showed a positive impact of RRF on anaemia management. Haemoglobin levels were significantly higher in HD patients with RUV than in anuric counterparts (Ma & Ding, 2013). Preserved RUV was negatively associated with ESA dose and ESA resistance index (Shafi et al., 2010; Teruel-Briones et al., 2013). ESA resistance index was also found to be 31% lower in patients with high rGFR (>4.13ml/min/1.73m2) than in patients without diuresis (Penne et al., 2011). Malyszko et al. (2006) found that serum hepacidin levels, which might indicate better iron store and erythropoesis, were significantly correlated to RRF in HD patients. These research findings indicate that RRF is associated with better anaemia management, which possibly improves anaemia-related poorer outcome in MHD patients.

Better nutrition

HD patients with RRF were indicated to have better nutritional status. Both RUV and rCLurea were found to be significantly associated with serum albumin levels whilst dCLurea was not associated (Suda et al., 2000; Yang et al., 2009). Both baseline and preserved RUV (≥200ml/day) were associated with a higher level of normalised total protein catabolic rate (Suda et al., 2000). Patients with preserved RRF tended to have more body fat and fat free body mass as well as a higher body mass index (Stolic et al., 2012; Suda et al., 2000). The better nutrition outcome is probably attributed to RRF-conferrer reduced inflammation, improved appetite, more freedom with diet...
choice and possibly better protein and fat metabolism (Suda et al., 2000; Yang et al., 2009).

**Better quality of life**

HD patients with RRF may have better QOL. The decline in rGFR is significantly associated with a worsening in health-related QOL (Poulson et al., 2017). Baseline RUV was associated with better QOL both at baseline and at 1 year follow-up, and patients with preserved RRF tended to have a better body image and less HD-related symptoms (Shafi et al., 2010). High rCLurea and RUV was also found to be correlated to lower depressive symptoms (Chilcot et al., 2009). The RRF-correlated improved QOL is likely brought by the associated preservation of overall health and wellbeing (Chilcot et al., 2009; Shafi et al., 2010).

**Factors impacting RRF**

After the initiation of dialysis, RRF continues to decrease and eventually disappears in most patients. Understanding current evidence regarding RRF decline in HD patients will assist nephrology nurses in preserving RRF in this population. Several factors that negatively impact on the deterioration of RRF have surfaced from studies in recent years. The important factors include IDH, inflammation, hypervolaemia and dialyser bio-incompatibility. Each of them will be discussed in detail.

**IDH**

IDH and end organ ischaemic damage has been deemed to be one of the major causes accelerating RRF decline in HD patients (Lang et al., 2001; Jansen et al., 2002; Schiffl et al., 2013). The slower decline of RRF among patients on continuous ambulatory PD (CAPD) compared to those on HD can be attributed to CAPD-related better cardiovascular stability (Lang et al., 2001). A combination of PD (5 days/week) and HD (once a week) therapy was reported to preserve RUV in 13 incident dialysis patients, and minimal fluid removal during HD was indicated as a major contributor (Ueda et al., 2017). Meanwhile, it was reported that more frequent hypotensive episodes in HD treatment contributed to a faster decline of RRF in HD patients as compared to HDF patients (Schiff et al., 2013). Since ultrafiltration rate (UFR) being faster than vascular refill is a major cause of IDH (Brown et al., 2015; Ok et al., 2017), two small studies investigated the effect of no fluid removal HD on RRF. Hyodo and Kotouku (2011) performed no fluid removal HD on 28 participants when IDWG was ≤2% of dry weight (DW) and found out that RUV was better preserved without subsequent significant fluid overload. Liu et al. (2014) conducted no fluid removal HD for 28 incident patients with RUV≥1,000ml/day, and discovered that no fluid removal did slow the decline of renal clearance of creatinine and RUV, but at the cost of worsened hypertension, LVH and cardiothoracic ratio. Limited UF was also an important factor together with diuretic agents in preserving RRF in a small cohort of seven patients (Sjolund et al., 2016). In comparison, strict volume control, achieved by salt restriction and lowering post weight 0.5–1.0kg than previous post weight as tolerated, was linked to a more rapid deterioration in RUV despite that also leading to better BP control, improved LVH and left ventricle ejection fraction (Gunal et al., 2004). It is possible that rapid weight reduction led to increased risk of intradialytic end organ hypoperfusion. IDH and end organ hypoperfusion, mainly caused by high UFR, may lead to ischaemic damage on remnant nephrons and accelerate the deterioration of RRF.

**Inflammation**

Among HD patients, whilst RRF was associated with a lower level of inflammation markers, inflammation was indicated as a detrimental factor accelerating the decline of RRF. Higher levels of serum inflammation makers such as C-reactive protein (CRP) and interleukin 6 (IL6) were linked with faster deterioration of RRF (Palomo-Piñón et al., 2014; Schiffl et al., 2002). The protective effect of a more compatible dialyser and purer dialysate on RRF was attributed to reduced systemic inflammation (McKane et al., 2002; Schiffl et al., 2002). Low grade systemic inflammation, a common phenomenon among HD patients, may hasten the decline of RRF.

**Hypervolaemia**

Hypervolaemia is suggested to have a negative impact on RRF. Several studies indicated that among patients on PD, hypervolaemia aggravates the decline of RRF as compared to euvoaemia (Rhee et al., 2016; McCafferty et al., 2013; Davenport et al., 2011; Tian et al., 2016). Hypervolaemia results in intestinal oedema and subsequent bacterial and endotoxin translocation into the blood stream, causing systemic inflammation which negatively impacts on RRF (Hassan et al., 2016; Dekker et al., 2017; Jacobs et al., 2010). Hypervolaemia, independently from its negative cardiovascular impact, may aggravate the decline of RRF.

**Dialyser bio-incompatibility**

Dialyser bio-incompatibility potentially negatively impacts on RRF. Improvements in dialyser biocompatibility were among the major factors slowing down the decline of RRF among HD patients (McKane et al., 2002). Blood membrane contact induces platelet and complement activation which leads to inflammation and oxidative organ damage including the kidneys (Daugirdas et al., 2013). With more biocompatible dialysers, complement and platelet activation has significantly decreased but still exists at varying degrees (Daugirdas et al., 2013; Hartman et al., 1997; Lang et al., 2001; Nilssen et al., 2007). Frequent nocturnal HD caused significantly more patients to completely lose RRF compared to thrice weekly standard HD (Daugirdas et al., 2013). The much longer weekly blood membrane contact (48 hours versus 12 hours) could be an important factor (Obi et al., 2016b). Further research is needed.
to shed more light on the impact of dialyser bio-incompatibility on RRF.

Strategies preserving RRF

In the last decade, increasingly more studies have been conducted regarding effective methods to preserve RRF for HD patients. The strategies that have been indicated as effective in research reports will now be discussed.

Incremental HD

Incremental HD has been indicated as preserving RRF (Liu et al., 2019). Incremental HD is a personalised HD prescription which allows for initial use of shorter hours and/or lower frequency for patients with substantial renal solute clearance and urine output (Mathew et al., 2018). A meta-analysis of 16 studies showed that incremental HD preserves both renal solute clearance and urine volume whilst providing equal or better outcome for patients with substantial RRF compared to standard thrice weekly HD (Liu et al., 2019). Both NKF-KDOQI Clinical Practice Guidelines and EBPG Guidelines for HD recommended converting rCLurea into Kt/V and then incorporating this into HD prescription (EBPG Working Group, 2002; National Kidney Foundation, 2015); this further supports that incremental HD may be beneficial for patients with RRF.

HDF

Two small studies suggested that HDF may slow the decline of RRF. Schiﬀi et al. (2013) found out that the rate of renal clearance of creatinine and RUV declining was much slower among patients on HDF. However, the ﬁndings were partially confounded by two types of dialyse with diﬀerent microbial purity, endotoxin content and dialysers with diﬀerent ﬂux being used in the study group and control group. Hyoto and Koutoku (2011) found that RUV declined much faster in patients on HD than that among patients on HDF in a trial without signiﬁcant confounding factors, in which correlation coeﬃciency between HDF vintage and RUV diminution (0.333) was signiﬁcantly lower than that between HD vintage and RUV decline (0.834). The HDF-preserving eﬀect can probably be explained by two HDF advantages. HDF is believed to maintain intradialytic BP better and reduce inﬂammation (Morena et al., 2017; Schiﬀi et al., 2013).

Pharmaceutical methods

Recent research has shown that some medications reduce the decline of RRF. Long-term use of diuretic agents may assist in preserving RRF among HD patients. Diuretics may not necessarily preserve rGFR, but enhance water and sodium excretion (Bragg-Gresham et al., 2007; Lemes et al., 2011; Sjolund et al., 2016). The improved ﬂuid status incurs less systemic inﬂammation. Moreover, it leads to less IDWG and subsequently lower UFR, thus avoiding the detrimental impact of high UFR-related intravascular volume depletion on RRF (Ok et al., 2017; Sjolund et al., 2016). N acetyl cysteine (NAC), a strong anti-oxidant, a nutrition supplement and a mucolytic drug, may have a favourable eﬀect on preserving RRF among HD patients with long-term use according to two small studies (Ahmadi et al., 2017; Feldman et al., 2012). The research of the impact of renin-angiotensin-aldosterone system blockade agents on RRF among HD patients yielded inconsistent results (Itoh et al., 2012; Kjaergaard et al., 2014; Mokoli et al., 2018; Xydakis et al., 2012). Iodinated contrast, some non-steroidal anti-inﬂammatory drugs and aminoglycoside antibiotics were generally considered as nephrotoxic agents, but there was insuﬃcient evidence to prove these agents aggravate the decline of RRF after the initiation of HD (Janousek et al., 2010; Bailie et al., 2004; Gooch et al., 2007; Patel & Hu, 2015).

Clinical practice implications

Based on currently available evidence, the following nursing practice implications can be suggested to preserve RRF for HD patients (Table 1).

IDH prevention

Preventing IDH is crucial in preserving RRF for HD patients as it is a major HD-related factor causing faster decline of RRF (Jansen et al., 2002; Lang et al., 2001; Schiﬀi et al., 2013; Kjaergaard et al., 2011). IDH is a multifactorial and detrimental intradialytic complication, the prevention of which requires a combination of methods. Educating and motivating patients to limit salt and ﬂuid intake prevents large IDWG (Brown et al., 2015; Ok et al., 2017). Facilitating patients’ adherence to diuretic medications enhances renal water and sodium excretion (Sjolund et al., 2016). For patients with substantial RUV, performing no or low ﬂuid removal is beneﬁcial (Sjolund et al., 2016; Hyoto & Koutoku 2011; Ok et al., 2017). Improving DW accuracy decreases the risk of hypovolaemia-related IDH, thorough physical examination and utilising aids such as multi-frequency bioimpedance spectroscopy, ultrasound and x-ray may improve DW accuracy (Dekker et al., 2017; Hyoto & Koutoku 2011; Reeves & McCausland, 2018). For patients needing large ﬂuid removal, extending UF time to keep UFR≤10ml/kg/hour as UFR>10ml/kg/hour was signiﬁcantly associated with higher risk of IDH and mortality, utilising isolated UF (ISO-UF) and UF proﬁling when necessary (Brown et al., 2015; Chou & Kalantar-Zadeh, 2017; Dheenan & Henrich, 2001; Saran et al., 2006). Some patients are predisposed to IDH by cardiac co-morbidities or impaired BP compensatory regulation; individualised UFR and UF proﬁle may decrease the risk in this case (Reeves & McCausland, 2018). Utilising other dialysis techniques like decreasing dialysate temperature and tuning UFR by blood volume monitoring helps prevent IDH (Bradshaw & Bennett, 2015; Brown et al., 2015; Hyoto, & Koutoku, 2011). Timely prompting antihypertensive medication
review and modification as patients’ fluid status and blood pressure improves can decrease medication-related IDH (Ok et al., 2017). Restricting intradialytic food intake decreases splanchnic blood flow and helps prevent IDH (Reeves & McCausland, 2018). Watching for subtle symptoms like tachycardia, palpitation and perspiration and using better BP indicators like mean arterial pressure and net BP changes may capture IDH early signs (Bradshaw & Bennett, 2015; Chou & Kalantar-Zadeh, 2017). Adopting pre-emptive methods like pausing or decreasing UFR can effectively prevent IDH (Bradshaw & Bennett, 2015). In the case of IDH occurring, prompt intervention like stopping UF, Trendelenberg’s position and fluid resuscitation is warranted to minimise the detrimental impact (Reeves & McCausland, 2018).

Volume control

Hypervolaemia may aggravate RRF declining apart from its long-term cardiovascular consequence (Chou et al., 2018; Rhee et al., 2016; Tian et al., 2016). As mentioned above, improving patients’ adherence to salt and fluid restriction will prevent or improve volume overload. Increasing DW accuracy is essential to prevent and correct inconspicuous hypervolaemia (Chou & Kalantar-Zadeh, 2017; Ok et al., 2017). IDH and intradialytic cramp, likely being caused by a vascular refilling rate lower than UFR, cardiac co-morbidities or an impaired blood pressure compensating mechanism, does not necessarily mean patients have reached DW, neither is absence of peripheral oedema necessarily a sign of euvolaemia (Ok et al., 2017; Reeves & McCausland, 2018). Instead, hypertension indicates hypervolaemia in most patients on HD (Ok et al., 2017). For patients with fluid overload, DW needs to be decreased gradually and slowly to avoid high UFR and rapid weight reduction-related IDH and ischaemic organ damage (Chou & Kalantar-Zadeh, 2017; Ok et al., 2017). It is suggested that decreasing DW by 0.2-0.3kg/session may be safer (Ok et al., 2017). Extra UF or ISO UF time is warranted for patients with severe hypervolaemia to correct volume overload whilst avoiding IDH (Saran et al., 2006).

Incremental HD

Observational studies showed that incremental HD may preserve RRF (Liu et al., 2019). Clinical teams can advocate and promote incremental HD for patients with substantial RRF. For patients on incremental HD, preventing large IDWG is important as shortened treatment time can result in high UFR and IDH. In the case of hypervolaemia, extra time for UF or ISO-UF needs to be added to keep the UFR at a tolerable range (Dheenan & Henrich 2001; Mathew et al., 2018). RRF will progressively and sometimes precipitously decline, and an insufficient dialysis dose causes a worse outcome in patients without sufficient RRF (Obi et al., 2016a; Wang et al., 2018). Clinical teams need to regularly monitor RRF and closely observe patients’ symptoms, serum markers and fluid status to timely facilitate HD dose increment (Mathew et al., 2018; National Kidney Foundation, 2015; Obi et al., 2016b).

Decreasing inflammation

Low grade systemic inflammation among HD patients is related to a myriad of preventable factors apart from renal failure itself. Short bacteria DNA fragments, which can freely cross dialyser membrane and likely originate from dialysate, were found in some HD patients’ blood and were associated with significantly higher CRP and IL6 levels (Bossola et al., 2009). Strategies to prevent dialysate microbial contamination and ensure the purity will decrease relevant inflammation. HD catheter access is prone to bacterial colonisation which is associated with faster loss of RRF due to the induced inflammation (Kang et al., 2016). Strict aseptic technique and promoting arterial-venous fistula usage will prevent the negative impact of dialysis catheter bacteria colonisation on RRF. Preventing hypervolaemia and dehydration can minimise inflammation originating from volume derangement (Dekker et al., 2017; Hassan et al., 2016; Jacobs et al., 2010; Yoo et al., 2017). It is also plausible to postulate that better infection control will minimise microorganism-related systemic inflammation. A systematic approach, aiming at the myriad causes, may decrease inflammation and minimise the negative impact on RRF.

Further considerations

Given the available evidence regarding the impact of PD, HDF, dialyser biocompatibility and some medications on RRF, some modifications in nursing practice may help slow the decline of RRF. Since less IDH corresponds to better preserved RRF in patients on PD (Lang et al., 2001; Jansen et al., 2002), advocating for more patients to choose PD modality or the combination of PD and HD therapy at the initiation of dialysis, and facilitating conversion to PD or the combination of PD and HD from HD for patients susceptible to IDH may assist in preserving RRF (Ueda et al., 2017). HDF may decrease systemic inflammation and bring better cardiovascular stability, thus benefiting RRF (Hyoto & Koutoku, 2011; Morena et al., 2017; Schifft et al., 2013). Advocating conversion from HD to HDF for patients with RRF may slow the declining. Dialyser bio-incompatibility negatively impacts on RRF due to the induced inflammation, and new dialysers with further improved biocompatibility like hydrophilic-coated membrane dialysers are emerging (Hartman et al., 1997; Kodama et al., 2017; McKane et al., 2002). Promoting more biocompatible dialysers might assist in RRF preservation. Advocating diuretic prescription and promoting patients’ adherence might help with preserving RRF (Bragg-Gresham et al., 2007; Lemes et al., 2011; Sjolund et al., 2016). NAC may also assist in preserving RRF; clinical teams can encourage patients to discuss the usage of NAC with their nephrologists (Ahmadi et al., 2016; Feldman et al., 2012).
Conclusion

RRF confers a wide range of powerful benefits and significantly better outcomes for patients on HD. Its progressive decline after the initiation of HD is associated with many factors. IDH, inflammation, hypervolaemia and dialyser bio-incompatibility are all important factors indicated by research to negatively impact on RRF, whilst incremental HD, HDF, PD modality and some medications have been suggested to slow the decrease of RRF. Based on the currently available evidence, nephrology nurses can improve everyday practice by preventing IDH, improving fluid status, optimising infection control and promoting incremental HD, HDF, PD or the combination of HD and PD to preserve RRF for patients on HD.

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Conflict of interest

The authors declare no conflicts of interest.

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References


Table 1. Summary of clinical practice implications

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<tr>
<th>Strategies</th>
<th>Practice implications</th>
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<tr>
<td>IDH prevention</td>
<td>• No or low intradialytic fluid removal for patients with substantial RUV.</td>
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<td></td>
<td>• Keep UFR ≤ 10ml/kg/hour.</td>
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<td>• Utilise ISO-UF and UF profiling.</td>
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<td></td>
<td>• Individualise UFR and UF profiling for patients prone to IDH.</td>
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<td>• Tune UFR by blood volume monitoring.</td>
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<td>• Decrease dialysate temperature.</td>
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<td>• Improve DW accuracy.</td>
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<td>• Improve patients’ salt and fluid restriction to avoid large IDWG.</td>
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<td>• Restrict intradialytic food intake.</td>
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<td>• Prompt antihypertensive medication review and modification.</td>
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<td>• Watch for IDH early signs and take pre-emptive methods.</td>
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<td></td>
<td>• Promptly treat IDH when it occurs.</td>
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<tr>
<td>Volume control</td>
<td>• Improve salt and fluid restriction.</td>
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<td></td>
<td>• Improve DW accuracy.</td>
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<td>• Gradually and gently decrease DW.</td>
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<td>• Extra time for UF or ISO-UF when necessary.</td>
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<tr>
<td>Incremental HD</td>
<td>• Advocate for incremental HD.</td>
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<td></td>
<td>• Closely and regularly monitor RRF and patients’ symptoms to inform HD dose modification.</td>
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<tr>
<td></td>
<td>• Be vigilant against high UFR.</td>
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<tr>
<td></td>
<td>• Add extra time for UF or ISO-UF to lower UFR when needed.</td>
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<tr>
<td>Decrease inflammation</td>
<td>• Promote AVF use and minimise catheter access.</td>
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<td></td>
<td>• Monitor water quality and prevent water contamination.</td>
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<td></td>
<td>• Practice infection control.</td>
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<tr>
<td></td>
<td>• Avoid high UFR and hypovolaemia.</td>
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<td></td>
<td>• Address hypervolaemia.</td>
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<tr>
<td>PD modality</td>
<td>• Advocate and facilitate patients with CKD to choose PD or PD+HD at the initiation of dialysis.</td>
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<td>• Promote conversion to PD or PD+HD from HD for patients susceptible to IDH.</td>
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<tr>
<td>HDF</td>
<td>• Introduce and promote HDF modality.</td>
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<tr>
<td>Pharmaceutical methods</td>
<td>• Improve patients’ adherence of diuretic medications.</td>
</tr>
<tr>
<td>Dialyser biocompatibility</td>
<td>• Use dialysers with improved biocompatibility.</td>
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