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Randomized Control Trials

The impact of hemodiafiltration with endogenous reinfusion (HFR) on micronutrient status in patients undergoing maintenance hemodialysis: A randomized crossover trial

Bo Yang [a,1], Zewei Chen [b,1], Cheng Xue [c,1], Changhao Zhu [a], Dan Ye [a], Qing Shao [a], Fanzhou Zeng [a,*], Nanmei Liu [a,**]

[a] Department of Nephrology, Naval Medical Center of the People's Liberation Amy (PLA), Naval Medical University, Shanghai, China
[b] Department of Nephrology, The First Navy Hospital of Southern Theater Command, Zhanjiang, China
[c] Division of Nephrology, Shanghai Changzheng Hospital, Second affiliated hospital of Naval Medical University (Second military medical university), Shanghai, China

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SUMMARY

Background: Micronutrient deficiencies are common in patients undergoing maintenance hemodialysis (MHD), potentially contributing to adverse clinical outcomes. Hemodiafiltration with endogenous reinfusion (HFR) integrates convection, diffusion, and adsorption, potentially preserving essential nutrients better than traditional online hemodiafiltration (HDF). This study aimed to compare the acute effects of HFR and HDF on serum micronutrient concentrations in MHD patients.

Methods: The research has been registered in chictr.org.cn (ChiCTR2500096698). In this randomized crossover trial, 30 adult MHD patients received one session each of HFR and HDF, separated by a 2-week washout period consisting of their standard maintenance hemodialysis. Blood samples were collected pre- and post-treatment for trace elements and vitamin concentrations. The primary outcome was post-treatment serum iodine concentration, chosen to assess the acute dialytic clearance efficiency of iodine. Secondary outcomes included changes in serum concentrations of other trace elements and water- and fat-soluble vitamins. Linear mixed models (LMM) were used for between-treatment comparisons, and paired tests for within-group changes.

Results: A total of 30 patients (mean age 55.7 ± 14.8 years; 63.3 % male) completed the study. No significant difference was observed in post-treatment serum iodine between HFR and HDF (adjusted mean difference: −0.019 μmol/L, $p = 0.343$). However, HFR was associated with significantly greater reductions in serum calcium, vitamin D3, and selenium, compared to HDF ($p < 0.05$ for all). In contrast, vitamin B3 concentrations were significantly higher after HFR ($p = 0.047$). No serious adverse events occurred, and both modalities were well-tolerated.

Conclusions: While HFR did not significantly differ from HDF in iodine clearance, it resulted in greater losses of calcium, vitamin D3, and selenium, but resulted in significantly higher post-treatment serum concentrations of vitamin B3. These findings suggest that until long-term studies demonstrate a clear net benefit, the routine clinical implementation of HFR outside of dedicated research contexts appears premature and requires significant caution.

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1. Introduction

The evolution of dialysis technology has profoundly transformed the management of end-stage kidney disease (ESKD), leading to substantial improvements in patient survival and quality of life [1–3]. Modern hemodialysis techniques have become increasingly sophisticated, effectively clearing uremic toxins and managing fluid balance [4,5]. However, despite these

* Corresponding author. Department of Nephrology, Naval Medical Center of PLA, Naval Medical University, Shanghai, China.
** Corresponding author. Department of Nephrology, Naval Medical Center of PLA, Naval Medical University, Shanghai, China.
E-mail addresses: zengfanzhou0622@126.com (F. Zeng), 13585996275@163.com (N. Liu).
[1] Bo Yang, Zewei Chen, and Cheng Xue contributed equally to this work.

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advancements, current modalities fail to fully replicate the intricate physiological functions of healthy kidneys [6]. Notably, the reabsorption of essential nutrients and the endocrine functions, vital for maintaining metabolic equilibrium, remain incompletely addressed [7]. Consequently, patients undergoing maintenance hemodialysis (MHD) continue to grapple with significant metabolic disturbances, including prevalent and often severe micronutrient deficiencies [8,9]. These deficiencies contribute to a spectrum of adverse outcomes, encompassing increased cardiovascular risk, compromised immune function, and diminished overall well-being, underscoring the critical need for improved dialysis strategies [10,11].

To address these inherent limitations, hemodiafiltration with endogenous reinfusion (HFR) has emerged as a promising innovation in renal replacement therapy. This technique integrates the complementary principles of diffusion, convection, and adsorption, offering a more holistic approach to solute removal and fluid management [12]. A defining characteristic of HFR is the incorporation of a specialized adsorbent cartridge, containing a strategic combination of resin and charcoal. This unique cartridge plays a pivotal role in the regeneration of ultrafiltrate, effectively converting it into an endogenous substitution fluid. By utilizing the patient's own filtered plasma, HFR aims to minimize the loss of essential substances, such as micronutrients and proteins, while simultaneously enhancing the clearance of uremic toxins. This approach holds the potential to mitigate the metabolic perturbations commonly observed in MHD patients.

Prior investigations have provided compelling evidence that HFR exhibits superior efficacy in reducing the concentrations of specific uremic toxins, particularly middle molecules, compared to conventional hemodiafiltration (HDF) [12–15]. These findings suggest that HFR may offer improved clearance of substances implicated in uremic toxicity and associated complications. Building upon this demonstrated efficacy in toxin removal and considering the mechanistic principles of HFR, which emphasize the preservation of endogenous substances through ultrafiltrate regeneration, it is hypothesized that HFR may also offer enhanced retention of crucial micronutrients compared to traditional HDF.

Therefore, this randomized controlled trial aims to comprehensively investigate the impact of HFR on micronutrient status in patients undergoing MHD. Specifically, we seek to determine whether HFR can effectively preserve essential micronutrients, including trace elements and vitamins, thereby potentially improving the overall metabolic profile and clinical outcomes in this vulnerable patient population. By elucidating the effects of HFR on micronutrient homeostasis, this study seeks to provide valuable insights that may inform clinical practice and contribute to the development of more effective dialysis strategies for patients with ESKD. Given that patients with ESKD are largely dependent on dialysis for iodine clearance, the primary aim of this trial was to compare the acute efficiency of HFR versus HDF in removing iodine from the blood, a direct measure of dialytic performance.

2. Methods

The protocol of the current study has been published [16]. The research has been registered in chictr.org.cn (ChiCTR2500096698).

2.1. Sample size

Sample size calculation was performed using G*Power 3.1 software. The calculation was based on an effect size of 0.45 taken directly from the cited pilot study by Lu et al. [17], which compared HFR and HDF for uremic toxin removal. As the specific means and standard deviations used to calculate this effect size were not detailed in their publication, we proceeded with the reported standardized effect size, a common practice in power calculations. To achieve 80 % power at a significance level of 0.05, 26 participants were required; 30 were recruited to allow for dropouts.

2.2. Inclusion and exclusion criteria

Eligible patients were ≥18 years old, receiving maintenance hemodialysis (HD) three times per week at the Naval Medical Center of People's Liberation Army, and had provided informed consent. Exclusion criteria included combined HD and peritoneal dialysis, recent (<1 week) surgery under general anesthesia, unstable clinical conditions, known malignancy or severe liver disease, and inability to eat orally.

2.3. Baseline data collection

Prior to intervention, baseline data were collected. This included demographics (sex, age), clinical background (primary renal disease, dialysis vintage, comorbidities), and anthropometrics. Height was measured once at baseline, while patient dry weight was assessed prior to each study session. Laboratory parameters included iron metabolism markers, BNP, CRP, BUN, total cholesterol, and hemoglobin. For the purpose of nutritional assessment, baseline serum albumin and prealbumin were measured. Nutritional status was further assessed using the Nutritional Risk Screening (NRS-2002) score, calculated from baseline data including BMI and age, with a severity of disease score of 2 assigned for chronic dialysis [18]. Other parameters included corrected calcium, phosphorus, and parathyroid hormone. The use of all medications and supplements was also recorded; while no participants were taking general multivitamin supplements, a subset of patients were receiving prescribed cholecalciferol (vitamin D3) as part of their routine clinical care.

2.4. Randomization and blinding

After a two-week HD washout, during which patients continued their usual, stable maintenance hemodialysis prescription, participants were randomized 1:1 into Arm A or B using a computer-generated sequence (Microsoft Excel for MacOS, Version 16.94) concealed in opaque envelopes. Intervention providers were unblinded, but outcome assessors and statisticians remained blinded.

Arm A: HDF (240 min) → 2-week HD washout → HFR (240 min).

Arm B: HFR (240 min) → 2-week HD washout → HDF (240 min).

Treatment days were designated as Day D (HDF) or Day R (HFR), with preceding HD sessions on Day D-2 or R-2.

2.5. Interventions

All sessions used low molecular weight heparin for anticoagulation, a minimum blood flow rate of 200 mL/min (target 250–350 mL/min if tolerated), dialysate flow of 500 mL/min, and a fixed duration of 240 min. Ultrafiltration volumes were individualized, generally limited to ≤5 % of dry weight.

2.6. Safety monitoring

Patients were monitored during dialysis for vital signs and circuit pressures. Treatment was discontinued in cases of severe hypotension, allergic reactions, access issues, clotting, or other significant events. Incomplete sessions were excluded from analysis when appropriate.

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2.7. HDF and HFR protocols

HDF treatments were conducted using a Fresenius 5008S machine with an FX80 dialyzer, employing post-dilution online HDF. HFR treatments were performed using the Formula Dialysis Therapy machine (Bellco, Italy) with the Supra17 filter and Suprasorb resin column.

2.8. Outcome measures

2.8.1. Blood sampling

Blood samples were collected immediately before and after each treatment, following KDOQI guidelines [19,20]. Post-treatment samples were drawn after dialysate flow cessation and brief reduction of blood flow. Analyses were performed at Kingmed Diagnostics (Guangzhou, China).

2.8.2. Primary outcome

Change in serum iodine (measured by ICP-MS). The primary outcome was serum iodine, selected not as a marker of chronic nutritional status, but as a direct measure of the acute dialytic clearance efficiency of a given dialysis modality. This is particularly relevant in ESRD patients who have lost the primary renal pathway for iodine elimination and are dependent on dialysis for its removal.

2.8.3. Secondary outcomes

Minerals and trace elements (Cu, Mg, Zn, Se, Fe, Ca, Pb, Cd by ICP-MS). Cd and Pb were included to assess the clearance of common environmental heavy metals that are known to accumulate in dialysis patients in certain circumstance.

Water-soluble vitamins (vitamins B2, B3, B5, B6, B9, and B12 by HPLC-MS/MS; and vitamin B7 by HPLC).

Fat-soluble vitamins (vitamin E by UHPLC; vitamins K, D2, D3 by HPLC-MS/MS).

2.9. Statistical analysis

Descriptive statistics were used to summarize baseline characteristics of the participants and outcome measures. Continuous variables were expressed as mean ± standard deviation (SD) if normally distributed, or median and interquartile range (IQR) if not normally distributed. Categorical variables were presented as frequency and percentage (%). Normality of data distribution, particularly for difference scores (post-treatment minus pre-treatment values), was assessed using the Shapiro–Wilk test to guide the choice of statistical tests for within-group changes.

Baseline demographic and clinical characteristics were compared between the two randomization sequence groups (Arm A vs. Arm B) using independent samples t-tests or Mann–Whitney U tests for continuous variables, and Fisher's exact test for categorical variables, to assess baseline comparability.

The primary method for comparing the effects of HFR versus HDF on the primary outcome (serum iodine) and all secondary micronutrient outcomes was the Linear Mixed Model (LMM). For each micronutrient, the post-treatment concentration was the dependent variable. The LMM included fixed effects for treatment (HFR vs. HDF), period (Period 1 vs. Period 2), and sequence (Arm A vs. Arm B). Covariates included in the model were the pre-treatment concentration of the specific micronutrient, ultrafiltration (as a percentage of body weight), dialysis vintage, age, and sex. A random intercept for participant was included to account for within-subject correlation, and a Compound Symmetry covariance structure was specified for the repeated measures. The LMM was used to estimate the adjusted mean difference in post-treatment micronutrient concentrations between the HFR and HDF interventions.

Changes in micronutrient concentrations from pre-to post-treatment within each treatment arm (HDF and HFR separately) were also assessed. Paired t-tests were used if the difference scores were normally distributed; otherwise, the Wilcoxon signed-rank test was applied. Specifically, for the primary outcome (serum iodine), within-group changes were analyzed using the Wilcoxon signed-rank test.

All secondary outcomes were also analyzed using LMM for between-treatment comparisons and the appropriate paired tests for within-group changes. Given the number of secondary outcomes, these analyses were considered exploratory. Adjustments for multiple comparisons (e.g., Bonferroni correction or False Discovery Rate [FDR]) were considered for selected secondary outcomes, and both adjusted and unadjusted p-values would be reported where applicable. Model assumptions for LMM (e.g., normality of residuals) were checked, and results were interpreted accordingly.

A two-sided p-value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS Statistics for MacOS (Version 30.0.0.0, IBM Corp., Armonk, NY). Study data were securely stored and accessible only to authorized study personnel.

3. Results

3.1. Participant flow

A total of thirty-eight participants were screened for eligibility, of whom 30 were randomized. Fifteen participants were assigned to Arm A (HDF followed by HFR), and fifteen to Arm B (HFR followed by HDF). All 30 participants completed both treatment periods, and their data were included in the primary analysis. No participants discontinued the study. The flow of participants through the trial is detailed in Fig. 1.

3.2. Baseline demographics and clinical characteristics

The baseline demographic and clinical characteristics of the 30 participants are summarized in Table 1. The mean age of participants was 55.7 ± 14.8 years, 19 (63.3 %) were male, and the mean body mass index (BMI) was 23.2 ± 3.4 kg/m^2. The median dialysis vintage was 5.0 years (Interquartile Range [IQR], 2.8–10.5 years). Prevalent comorbidities included hypertension in 28 (93.3 %) patients, diabetes mellitus in 10 (33.3 %), and coronary heart disease (CHD) in 10 (33.3 %). The primary causes of kidney failure were glomerular disease (14 patients, 46.7 %), diabetic nephropathy (10 patients, 33.3 %), hypertensive nephropathy (2 patients, 6.6 %), and other causes (4 patients, 13.3 %). At enrollment, no statistically significant differences in baseline laboratory parameters were observed between Arm A and Arm B.

3.3. Effects of dialysis modality on micronutrient concentrations

The effects of HFR versus HDF on micronutrient concentrations were analyzed using LMM. These models included fixed effects for treatment, period, and sequence, with pre-treatment micronutrient concentration, ultrafiltration (as a percentage of body weight), dialysis vintage, age, and sex included as covariates. A random intercept for participant and a Compound Symmetry covariance structure were specified. Within-group changes from pre-to post-treatment for both HDF and HFR phases were assessed using paired t-tests, or Wilcoxon signed-rank tests if difference data were not normally distributed.

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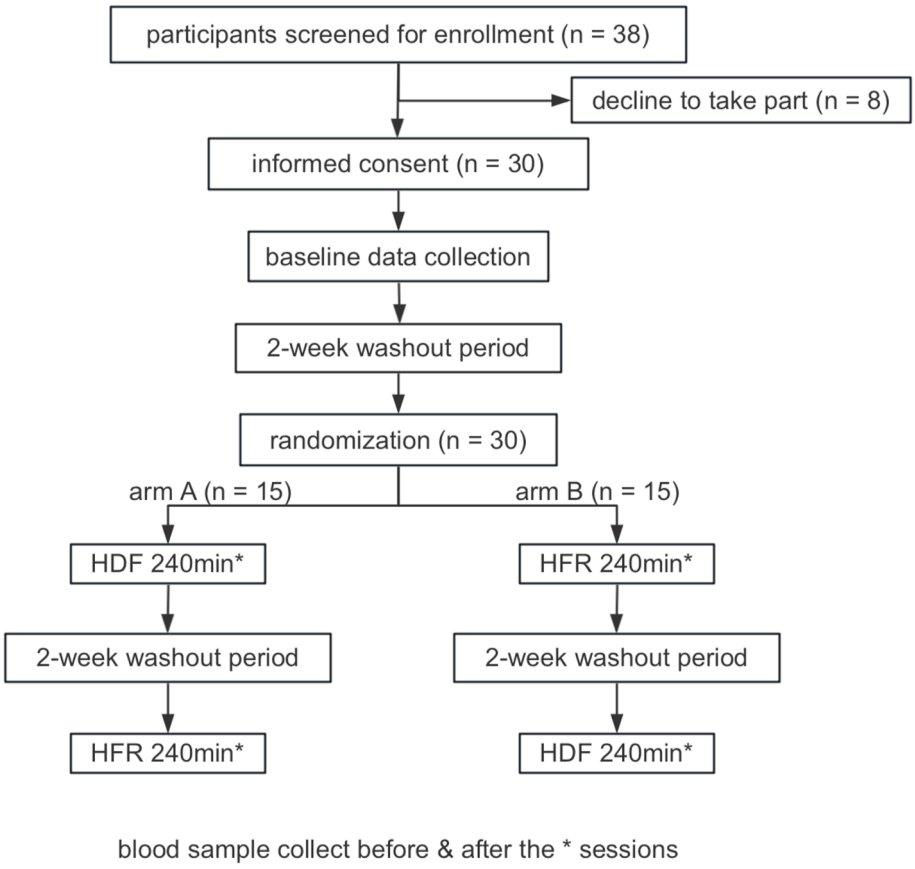

Fig. 1. Study flowchart.

Table 1
Baseline characteristics of the study participants.

Variables	All	Arm A (n = 15)	Arm B (n = 15)
Age (years), mean (range)	55.7 (24, 78)	54.0 (24, 71)	57.4 (33, 78)
Sex (men), n (%)	19 (63.3)	10 (66.7)	9 (60.0)
Dialysis vintage (years), median (IQR)	5.0 (2.8, 10.5)	5.0 (3.0, 13.0)	6.0 (2.0, 9.8)
BMI (kg/m^2), mean ± SD	23.2 ± 3.4	22.4 ± 3.2	23.9 ± 3.7
On cholecalciferol supplement	9	4	5
NRS-2002, median (IQR)	2 (2, 3)	2 (2, 2)	2 (2, 3)
Concomitant disease, n (%)			
Hypertension	28 (93.3)	14 (93.3)	14 (93.3)
Diabetes mellitus	10 (33.3)	5 (33.3)	5 (33.3)
coronary Heart disease	10 (33.3)	6 (40.0)	4 (26.7)
Cause of kidney failure, n (%)			
Glomerular disease	14 (46.7)	8 (53.3)	6 (40.0)
Diabetic nephropathy	10 (33.3)	5 (33.3)	5 (33.3)
Hypertensive nephropathy	2 (6.6)	0 (0)	2 (13.3)
Others	4 (13.3)	2 (13.3)	2 (13.3)
Laboratory tests			
BNP (pg/mL), median (IQR)	117.2 (57.8, 414.8)	117.0 (71.6, 1215.0)	100.0 (57.7, 206.1)
Pro-BNP (pg/mL), median (IQR)	2872.5 (1828.0, 6186.5)	3859.0 (2063.0, 35000.0)	2502.0 (1452.0, 4196.0)
Hemoglobin (g/L), mean ± SD	108.9 ± 16.9	106.5 ± 20.9	111.3 ± 12.0
C-reactive protein (mg/L), median (IQR)	2.3 (0.9, 4.9)	4.3 (1.0, 8.0)	1.8 (0.6, 4.0)
Total cholesterol (mmol/L), mean ± SD	3.4 ± 0.8	3.3 ± 0.9	3.5 ± 0.8
Albumin (g/L), mean ± SD	41.8 ± 3.4	42.3 ± 3.4	41.2 ± 3.3
Prealbumin (mg/L), mean ± SD	350.00 ± 87.35	319.91 ± 98.09	380.09 ± 65.13
Urea nitrogen (mmol/L), mean ± SD	24.1 ± 7.2	23.7 ± 3.4	41.2 ± 3.3
Calcium (mmol/L), mean ± SD	2.3 ± 0.2	2.2 ± 0.2	2.3 ± 0.2
Phosphate (mmol/L), mean ± SD	2.1 ± 0.6	2.0 ± 0.6	2.1 ± 0.6
Parathyroid hormone (pg/mL), median (IQR)	234.3 (39.9, 453.8)	224.8 (40.6, 365.0)	243.7 (37.7, 466.9)
Ferritin (ng/mL), median (IQR)	32.6 (21.2, 116.9)	30.1 (20.6, 120.6)	34.2 (22.8, 86.3)
Serum iron (μmol/L), median (IQR)	64.1 (41.6, 93.1)	43.9 (41.3, 84.2)	76.0 (58.9, 99.5)
Transferrin (g/L), mean ± SD	2.5 ± 0.5	2.5 ± 0.6	2.4 ± 0.5
Transferrin saturation (%)	24 ± 1.6	20 ± 1.1	29 ± 1.9

Arm A: HDF followed by HFR; Arm B: HFR followed by HDF; BMI: Body mass index; BNP: brain natriuretic peptide; NRS-2002: Nutrition Risk Screening 2002.

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Descriptive statistics, including pre-treatment, post-treatment, and change from pre-to post-treatment for key micronutrients, are presented in Table 2 and Figs. 2–4.

3.3.1. Primary outcome: serum iodine

No statistically significant difference was observed in post-treatment serum iodine concentrations between the HFR and HDF treatment modalities (Adjusted Mean Difference [HFR - HDF]: −0.019 μmol/L, 95 % CI: −0.060 to 0.022; F (1, 24.055) = 0.934, p = 0.343). The estimated marginal mean for post-treatment serum iodine was 0.52 μmol/L (95 % CI: 0.465–0.577 μmol/L) after HFR, and 0.54 μmol/L (95 % CI: 0.485–0.596 μmol/L) after HDF. Pre-treatment serum iodine was not a significant predictor of post-treatment serum iodine (F (1, 30.082) = 0.313, p = 0.580). No significant period effect (F (1, 24.192) = 0.785, p = 0.384) or sequence effect (F (1, 23.673) = 1.108, p = 0.303) was observed for serum iodine (Table 3 and Fig. 2).

Within-Group Changes (Pre-vs. Post-Treatment – Wilcoxon Signed-Rank Test): During the HDF treatment phase, serum iodine concentrations showed a non-significant change from pre-to post-treatment (median change: −0.01 μg/L, IQR: −0.07 to 0.55 μg/L; p = 0.530). During the HFR treatment phase, serum iodine concentrations showed a statistically significant decrease from pre-to post-treatment (median change: −0.03 μg/L, IQR: −0.75 to 0.01 μg/L; p = 0.023).

3.3.2. Secondary outcomes

The LMM analysis of secondary micronutrient outcomes revealed several statistically significant differences between HFR and HDF treatments. Key findings and within-group changes are presented below. Comprehensive results for all secondary outcomes are detailed in Table 3.

3.3.3. Calcium, Vitamin D2, and Vitamin D3 homeostasis

Post-treatment concentrations of serum calcium, vitamin D2, and vitamin D3 were compared between modalities.

- Serum Calcium:

Comparison between HDF and HFR (LMM): Post-treatment serum calcium concentrations were significantly lower following HFR compared to HDF (Adjusted Mean Difference [HFR - HDF]: −3.29 mg/L, 95 % CI: −5.18 to −1.39 mg/L; p = 0.001). The estimated marginal mean for post-treatment calcium was 66.03 mg/L (95 % CI: 64.26, 67.80) for HFR and 69.32 mg/L (95 % CI: 67.56, 71.07) for HDF (Table 3 and Fig. 2).

Within-Group Changes (Paired t-test): Serum calcium concentrations significantly increased from pre-to post-treatment during both the HFR phase (mean change: 1.85 mg/L, p = 0.019) but increased after the HDF phase (mean change: 4.77 mg/L, p = 0.001).

- Vitamin D2:

Comparison between HDF and HFR (LMM): Post-treatment Vitamin D2 concentrations were numerically lower following HFR compared to HDF, though this difference was not statistically significant (Adjusted Mean Difference [HFR - HDF]: −2.97 ng/mL, 95 % CI: −7.55 to 1.62 ng/mL; p = 0.194). The estimated marginal mean was 1.84 ng/mL (95 % CI: −0.593, 4.275) for HFR and 4.81 ng/mL (95 % CI: 2.395, 7.224) for HDF (Table 3 and Fig. 4).

Within-Group Changes (Wilcoxon Signed-Rank Test): Vitamin D2 concentrations significantly increased from pre-to post-treatment during the HDF phase (median change: 0.15 ng/mL, IQR: −0.100, 0.400, p = 0.025). In contrast, during the HFR phase, Vitamin D2 concentrations did not significantly change (median change: 0.00 ng/mL, IQR: −0.300, 0.225 p = 0.665).

- Vitamin D3:

Comparison between HDF and HFR (LMM): Post-treatment Vitamin D3 concentrations were significantly lower following HFR compared to HDF (Adjusted Mean Difference [HFR - HDF]: −0.91 ng/mL, 95 % CI: −1.81 to −0.01 ng/mL; p = 0.049). The estimated marginal mean was 14.27 ng/mL (95 % CI: 13.38, 15.15)

Table 2
Pre-treatment, Post-treatment, and within-group change in micronutrient concentrations by dialysis modality.

Parameters	HDF				HFR			
	Pre-HDF	Post-HDF	t (Z)	P-value	Pre-HFR	Post-HFR	t (Z)	P-value
Trace elements and minerals								
I (μmol/L), median (IQR)	0.54 (0.48, 0.61)	0.53 (0.42, 0.63)	0.628	0.530	0.52 (0.45, 0.63)	0.51 (0.40, 0.62)	2.276	0.023
Fe (mg/L), mean ± SD	384.7 ± 65.6	411.4 ± 74.7	−5.129	<0.001	376.0 ± 70.4	409.4 ± 83.8	−6.131	<0.001
Ca (mg/L), mean ± SD	64.1 ± 8.0	68.9 ± 7.1	−3.896	0.001	65.0 ± 8.7	66.8 ± 7.5	−2.474	0.019
Zn (mg/L), mean ± SD	6.0 ± 1.0	6.3 ± 1.2	−4.233	<0.001	5.7 ± 1.1	6.2 ± 1.3	−4.781	<0.001
Cu (μg/L), mean ± SD	925.6 ± 212.0	978.9 ± 215.2	−5.266	<0.001	892.1 ± 181.6	941.1 ± 184.9	−5.564	<0.001
Pb (μg/L), mean ± SD	49.8 ± 17.3	53.0 ± 18.4	−3.998	<0.001	48.9 ± 17.1	53.2 ± 19.7	−4.329	<0.001
Mg (mg/L), mean ± SD	45.0 ± 6.1	42.5 ± 5.5	4.221	<0.001	44.6 ± 6.0	42.2 ± 6.3	5.037	<0.001
Cd (μg/L), median (IQR)	1.9 (1.4, 2.4)	1.8 (1.4, 2.7)	−1.621	0.116	1.6 (1.3, 2.5)	2.0 (1.4, 2.4)	−2.658	0.008
Se (μg/L), mean ± SD	76.3 ± 17.2	82.4 ± 20.5	−3.230	0.003	75.2 ± 14.8	76.6 ± 19.1	−0.773	0.446
Water-soluble vitamins								
Vitamin B2 (ng/mL), median (IQR)	4.2 (2.5, 6.9)	3.8 (2.3, 9.3)	1.142	0.254	3.9 (2.7, 8.4)	3.9 (2.3, 8.0)	0.021	0.984
Vitamin B3 (ng/mL), mean ± SD	77.8 ± 38.1	98.7 ± 40.1	−2.355	0.025	69.4 ± 35.7	111.0 ± 40.6	−5.928	<0.001
Vitamin B5 (ng/mL), median (IQR)	81.5 (69.8, 98.0)	62.3 (52.1, 86.4)	4.762	<0.001	77.7 (66.2, 106.9)	70.9 (57.5, 92.7)	3.630	<0.001
Vitamin B6 (ng/mL), median (IQR)	2.5 (0.31, 5.4)	1.4 (0.58, 3.5)	1.594	0.111	2.7 (0.76, 5.7)	2.1 (0.47, 3.4)	1.697	0.090
Vitamin B7 (ng/mL), median (IQR)	1.9 (1.1, 3.8)	1.3 (0.79, 2.1)	2.911	0.004	2.0 (0.46, 4.2)	2.1 (0.94, 3.3)	0.895	0.371
Vitamin B9 (ng/mL), median (IQR)	4.8 (2.9, 11.7)	2.0 (1.2, 4.6)	4.741	<0.001	4.3 (2.8, 9.5)	2.6 (1.6, 4.1)	4.762	<0.001
Vitamin B12 (ng/mL), median (IQR)	0.32 (0.19, 0.72)	0.18 (0.12, 0.25)	3.904	<0.001	0.28 (0.18, 0.62)	0.15 (0.10, 0.28)	3.742	<0.001
Fat-soluble vitamins								
Vitamin D2 (ng/mL), median (IQR)	0.80 (0.48, 1.48)	0.80 (0.50, 3.2)	−2.242	0.025	0.85 (0.40, 1.6)	0.75 (0.48, 1.5)	0.422	0.665
Vitamin D3 (ng/mL), mean ± SD	14.1 ± 4.7	15.1 ± 5.4	−2.016	0.050	14.2 ± 5.1	14.0 ± 5.1	0.772	0.446
Vitamin E (μg/L), median (IQR)	10.1 (8.8, 11.4)	11.5 (8.3, 13.3)	−2.437	0.015	10.1 (8.0, 12.7)	10.8 (6.8, 14.7)	−1.903	0.057
Vitamin K1 (ng/mL), median (IQR)	0.62 (0.32, 1.13)	1.2 (0.58, 2.4)	−2.968	0.001	0.7 (0.4, 1.3)	1.3 (0.84, 2.3)	−3.918	<0.001

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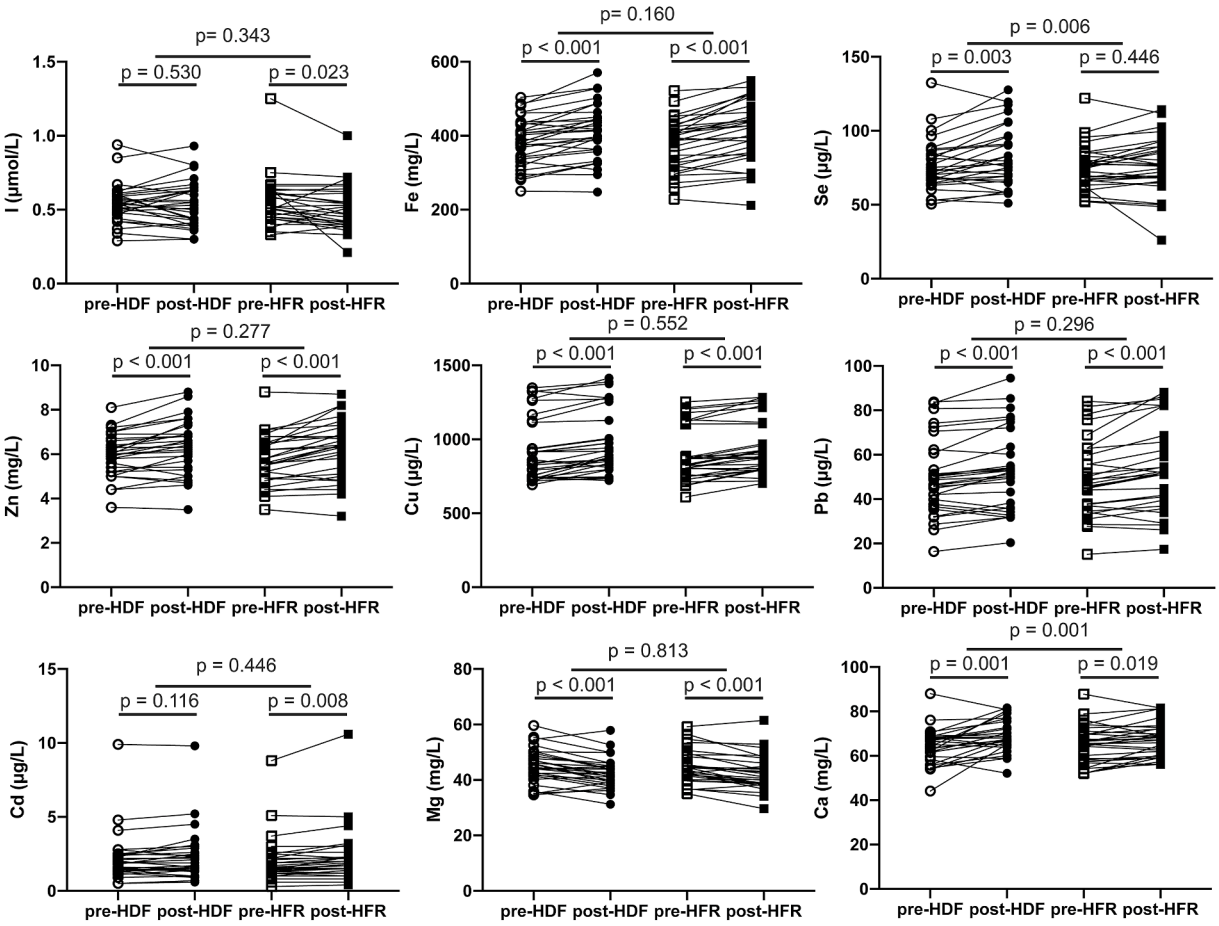

Fig. 2. Within-group changes and comparison between HDF and HFR on the trace elements and minerals.

for HFR and 15.18 ng/mL (95 % CI: 14.30, 16.05) for HDF (Table 3 and Fig. 4).

Within-Group Changes (Paired t-test): Vitamin D3 concentrations significantly increased from pre-to post-treatment during the HDF phase (mean change: 0.947 ng/mL, p = 0.050). During the HFR phase, Vitamin D3 concentrations did not significantly change (mean change: −0.230 ng/mL, p = 0.446).

3.3.4. Other key secondary outcomes

- Serum Selenium:

Comparison between HDF and HFR (LMM): HFR treatment was associated with a more pronounced decrease in serum selenium concentrations. Post-treatment selenium concentrations were significantly lower following HFR compared to HDF (Adjusted Mean Difference [HFR - HDF]: −4.24 μg/L, 95 % CI: −7.18 to −1.30 μg/L; p = 0.006). The estimated marginal mean was 77.01 μg/L (95 % CI: 73.08, 80.95) for HFR and 81.26 μg/L (95 % CI: 77.34, 85.17) for HDF (Table 3 and Fig. 2).

Within-Group Changes (Paired t-test): Serum selenium concentrations significantly increased from pre-to post-treatment during the HDF phase (mean change: 6.05 μg/L, p = 0.003). During the HFR phase, serum selenium concentrations did not significantly change (mean change: 1.39 μg/L, p = 0.446).

- Vitamin B3 (Niacin):

Comparison between HDF and HFR (LMM): HFR appeared to maintain Vitamin B3 concentrations more efficiently than HDF. Post-treatment Vitamin B3 concentrations were significantly higher following HFR compared to HDF (Adjusted Mean Difference [HFR - HDF]: 15.77 ng/mL, 95 % CI: 0.252–31.282 ng/mL; p = 0.047). The estimated marginal mean was 112.75 ng/mL (95 % CI: 98.355, 127.138) for HFR and 96.98 ng/mL (95 % CI: 82.753, 111.207) for HDF (Table 3 and Fig. 3).

Within-Group Changes (Paired t-test): Vitamin B3 concentrations significantly increased from pre-to post-treatment during both the HDF phase (mean change: 20.91 ng/mL, p = 0.025) and the HFR phase (mean change: 41.591 ng/mL, p < 0.001).

No statistically significant differences between HFR and HDF were observed for Fe, Zn, Cu, Pb, Mg, Cd, Vitamin B2, Vitamin B5, Vitamin B6, Vitamin B7, Vitamin B9, Vitamin B12, Vitamin E and Vitamin K1 (all p > 0.05; Table 3).

3.4. Safety and tolerability

Both HFR and HDF treatments were generally well-tolerated. A total of seven adverse events (AEs) were reported during the study: three AEs during HDF treatment periods and four AEs during HFR treatment periods. The most common AEs were hypotension (HDF: n = 1, HFR: n = 2) and muscle cramps (HDF: n = 2,

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Table 3
Comparison of post-treatment micronutrient concentrations between HRF and HDF using linear mixed models (LMM).

Parameters	EM mean HDF (95 % CI)	EM mean HFR (95 % CI)	Adjusted Mean Difference (HFR-HDF) (95 % CI)	F-statistic (Numerator df, Denominator df) (Treatment Effect)	p-value (Treatment Effect)
Trace elements and minerals					
I (μmol/L)	0.54 (0.49, 0.60)	0.52 (0.47, 0.58)	−0.02	0.934 (1, 24.055)	0.343
Fe (mg/L)	407.55 (396.85, 418.26)	414.86 (404.08, 425.63)	7.31	2.098 (1, 25.656)	0.160
Ca (mg/L)	69.32 (67.56, 71.07)	66.03 (64.26, 67.80)	−3.29	12.737 (1, 24.805)	0.001
Zn (mg/L)	6.24 (6.00, 6.48)	6.34 (6.09, 6.60)	0.10	1.235 (1, 24.109)	0.277
Cu (μg/L)	952.81 (934.51, 971.12)	947.01 (928.53, 965.49)	−5.81	0.363 (1, 27.122)	0.552
Pb (μg/L)	52.44 (47.49, 57.38)	53.517 (48.57, 58.47)	1.08	1.140 (1, 25.134)	0.296
Mg (mg/L)	42.38 (41.39, 43.36)	42.55 (41.54, 43.55)	0.17	0.057 (1, 21.873)	0.813
Cd (μg/L)	2.14 (2.01,2.26)	2.20 (2.08, 2.33)	0.07	0.600 (1, 25.406)	0.446
Se (μg/L)	81.26 (61.09, 101.42)	77.014 (56.84, 97.19)	−4.24	8.816 (1, 25.255)	0.006
Water-soluble vitamins					
Vitamin B2 (ng/mL)	11.35 (9.43, 13.26)	10.50 (8.57, 12.42)	−0.85	0.897 (1, 9.765)	0.367
Vitamin B3 (ng/mL)	96.98 (82.31, 111.65)	112.75 (97.92, 127.58)	15.77	4.353 (1, 26.674)	0.047
Vitamin B5 (ng/mL)	97.48 (87.27, 107.70)	99.14 (88.79, 109.50)	1.66	0.072 (1, 26.682)	0.791
Vitamin B6 (ng/mL)	2.02 (1.19, 2.84)	2.21 (1.37, 3.05)	0.19	0.084 (1, 25.723)	0.774
Vitamin B7 (ng/mL)	1.57 (−4.50, 7.64)	3.06 (−3.01, 9.13)	1.49	3.890 (1, 26.059)	0.057
Vitamin B9 (ng/mL)	6.60 (5.01, 8.18)	7.21 (5.60, 8.81)	0.61	0.433 (1, 21.731)	0.518
Vitamin B12 (ng/mL)	0.21 (0.14, 0.27)	0.196 (0.13, 0.26)	−0.01	0.213 (1, 24.364)	0.649
Fat-soluble vitamins					
Vitamin D2 (ng/mL)	4.81 (2.40, 7.22)	1.84 (−0.59, 4.28)	−2.97	1.771 (1, 27.292)	0.194
Vitamin D3 (ng/mL)	15.18 (11.97, 18.38)	14.27 (11.06, 17.47)	−0.91	4.351 (1, 21.900)	0.049
Vitamin E (μg/L)	11.50 (10.20, 12.80)	11.92 (10.60, 13.24)	0.42	0.186 (1, 26.348)	0.670
Vitamin K1 (ng/mL)	1.89 (1.27, 2.52)	1.88 (1.25, 2.52)	−0.01	0.001 (1, 15.014)	0.980

HFR: n = 2). No serious adverse events occurred during the trial. No dialysis sessions were discontinued prematurely due to adverse events.

4. Discussion

This randomized crossover trial aimed to compare the effects of HFR and online HDF on micronutrient status in maintenance hemodialysis (MHD) patients. Our study yielded several key findings. Firstly, for our primary outcome, we found no statistically significant difference in post-treatment serum iodine concentrations between HFR and HDF, although a significant decrease in iodine was observed from pre-to post-session within the HFR arm. Secondly, for secondary outcomes, HFR treatment was associated with significantly lower post-treatment concentrations of serum calcium, vitamin D3, and selenium compared to HDF. Conversely, HFR resulted in significantly higher post-treatment concentrations of vitamin B3 (niacin) than HDF. Post-treatment vitamin D2 concentrations were numerically lower with HFR but not statistically different from HDF. Many other investigated vitamins and trace elements did not differ significantly between the two modalities. It is important to note that some observed within-session increases in certain micronutrient concentrations may be partly influenced by hemoconcentration due to ultrafiltration, in addition to the specific clearance or preservation characteristics of each dialysis modality. To account for this, ultrafiltration volume was included as a covariate in our statistical models, thereby statistically controlling for the confounding influence of hemoconcentration.

4.1. Interpretation of findings and potential explanations

The absence of a significant difference in post-treatment serum iodine concentrations between HFR and HDF suggests that both modalities may have similar overall impacts on iodine during a single session, despite the theoretical potential of HFR to better

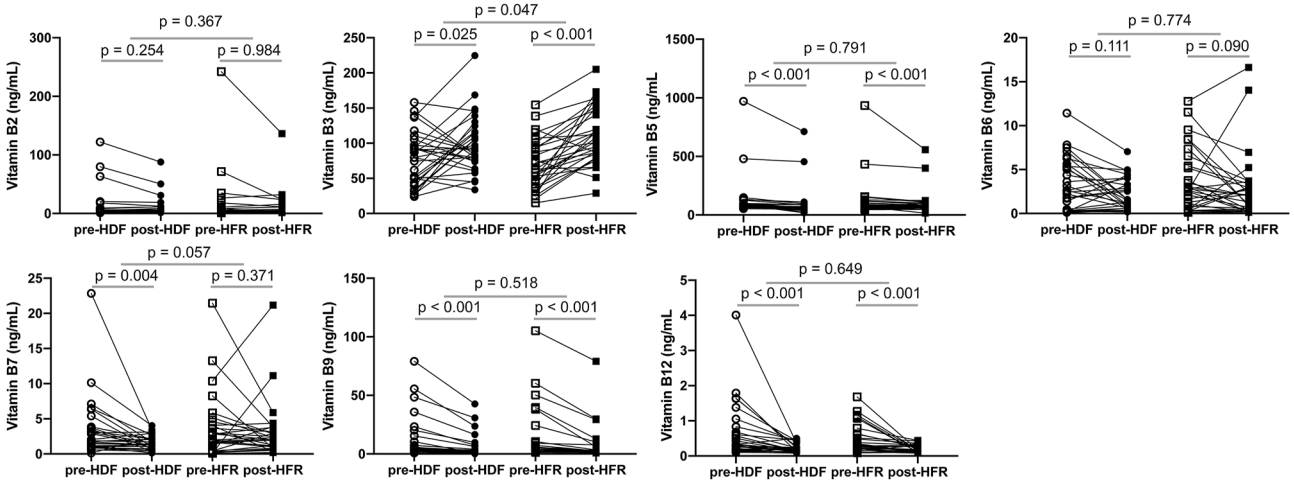

Fig. 3. Within-group changes and comparison between HDF and HFR on the water-soluble vitamins.

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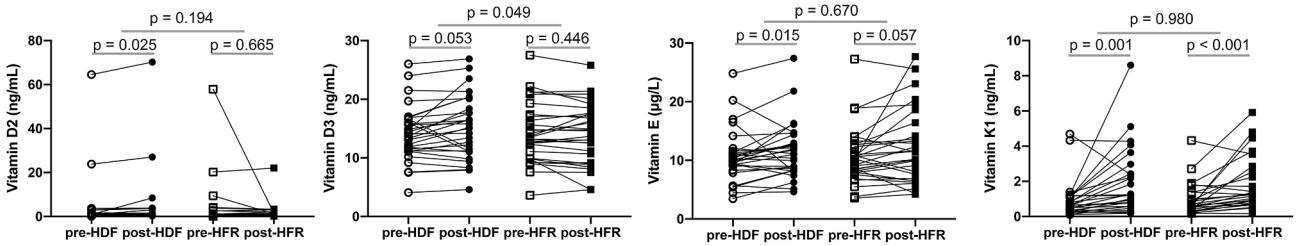

Fig. 4. Within-group changes and comparison between HDF and HFR on the fat-soluble vitamins.

preserve essential substances. The significant decrease in iodine observed within the HFR session, but not HDF, warrants further investigation. Iodine is a relatively small molecule, and its clearance can be influenced by dialyzer membrane characteristics, protein binding (though a significant portion is inorganic iodide), and dialysate iodine content, which was not controlled in this study [21,22]. The adsorbent cartridge in HFR, while designed to remove uremic toxins, might play a complex role; however, its specific interaction with iodine is not well-established and may not offer a significant advantage for iodine preservation over HDF in a single session context.

The more pronounced decreases observed in serum calcium, vitamin D3, and selenium with HFR compared to HDF are notable and somewhat counterintuitive to the hypothesis that HFR better preserves essential nutrients.

Calcium: The significantly lower post-treatment calcium with HFR could be influenced by several factors. While the LMM adjusted for pre-treatment concentrations, differences in calcium flux related to the specific characteristics of the HFR system, including potential binding to the adsorbent cartridge or altered kinetics due to the reinfusion process, might contribute [23,24]. It is also important to consider the dialysate calcium concentration used, which is standard across treatments but whose interaction with the regenerative process of HFR might differ. The finding that calcium increased within the HDF session but decreased within HFR highlights a differential impact that needs further exploration.

Vitamin D (D2 and D3): Vitamins D2 and D3 are fat-soluble and largely protein-bound, primarily to vitamin D-binding protein (VDBP) and albumin [25,26]. While protein-bound molecules are generally poorly cleared by dialysis, some free fraction exists. The resin component of the HFR Suprasorb cartridge is known to adsorb hydrophobic and protein-bound substances [12]. It is plausible that the cartridge might adsorb VDBP-bound or free vitamin D metabolites, or that the process alters VDBP concentrations or binding affinity, leading to enhanced net loss compared to HDF, where adsorption is not a primary clearance mechanism for such large molecules [27]. Although the difference for Vitamin D2 did not reach statistical significance, the trend was similar to the significant finding for Vitamin D3. The within-session increase in D2 and D3 during HDF is an interesting contrast and might reflect fluid shifts concentrating the plasma or release from stores, which seems less apparent or counteracted in HFR.

Selenium: Selenium is an essential trace element incorporated into selenoproteins. Its homeostasis in dialysis patients is complex [8,28]. The lower post-treatment selenium concentrations with HFR could potentially be due to adsorption of selenoproteins or inorganic selenium forms onto the HFR cartridge. The Suprasorb cartridge's mixed resin-charcoal composition might have an affinity for certain selenium species [29,30]. The observed significant increase within HDF compared to no significant change within HFR for selenium is complex and suggests the complexity of selenium handling by these advanced dialysis modalities and merit further investigation.

In contrast, the finding that HFR resulted in significantly higher post-treatment concentrations of Vitamin B3 (niacin) concentrations more efficiently than HDF is a positive signal. Niacin is a water-soluble B vitamin. Its better preservation with HFR could be attributed to the regeneration of the ultrafiltrate. If niacin is not significantly adsorbed by the Suprasorb cartridge, its reinfusion with the endogenous substitution fluid would lead to lower net losses compared to HDF, where convective losses might be higher without such a regenerative loop [31,32]. Both modalities showed a significant increase in Vitamin B3 post-session, with HFR showing a numerically larger increase, which aligns with the LMM finding of better maintenance with HFR.

For the numerous other micronutrients where no significant difference was found between HFR and HDF, it suggests that, under the conditions of this study, the specific mechanisms of HFR (including adsorption and reinfusion) did not lead to a markedly different net effect on these substances compared to the high convective and diffusive clearance of online HDF over a single session.

4.2. Clinical implications and decision making

The results of this study have several potential clinical implications. While HFR is known for its superior clearance of certain uremic toxins [12–15], its impact on micronutrient homeostasis appears to be complex and molecule-specific. The finding that HFR may lead to greater session decreases of calcium, vitamin D3, and selenium warrants careful consideration, particularly for patients already at risk for deficiencies or disturbances in mineral and bone metabolism or selenium-dependent enzyme functions [33,34]. Clinicians might need to monitor these micronutrients more closely in patients switched to HFR or consider targeted supplementation strategies if these findings are confirmed in longer-term studies.

These molecule-specific effects necessitate a more critical evaluation of HFR's overall role in clinical practice. The central question raised by our data is whether the reported benefits of HFR in clearing certain protein-bound uremic toxins outweigh the potential harm from increased session losses of essential micronutrients like calcium, vitamin D3, and selenium. Our findings suggest this is not a simple question of superiority, but a complex clinical trade-off. For a patient already struggling with mineral and bone disease, the greater loss of calcium and vitamin D3 could be clinically detrimental, potentially negating any benefits gained from toxin removal. This pattern of response complicates clinical decision-making and challenges the broader clinical value of this more sophisticated and costly technique compared to standard HDF.

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Conversely, the better preservation of vitamin B3 with HFR is a favorable outcome, as niacin has several beneficial roles, including in lipid metabolism and potentially vascular health [35]. If HFR consistently demonstrates better preservation of certain beneficial compounds alongside toxin removal, this could be an advantage for specific patient profiles.

The lack of difference for the primary outcome, iodine, and many other micronutrients suggests that for these substances, the choice between HFR and HDF may not be dictated by concerns over differential acute session losses, at least based on our findings. The decision to use HFR might therefore hinge more on its reported benefits in the clearance of certain uremic toxins, such as p-cresol and middle molecules [12–15], while being mindful of its potential impact on Ca, Vit D, and Se.

4.3. Discrepancy from study protocol

The published study protocol [16] indicated that repeated measures ANOVA was originally planned for the primary analysis. In the final analysis, LMM were employed. This decision was made because LMMs offer greater flexibility in handling covariates, modeling different covariance structures for repeated measures, and managing missing data (though no participants discontinued in this study), generally providing a more robust approach for crossover trial data [36]. This change in analytical strategy was deemed appropriate to best address the study objectives with the collected data.

4.4. Limitations of the study

This study has several strengths, including its randomized crossover design, which minimizes inter-patient variability, and the blinding of outcome assessors and statisticians. However, some limitations should be acknowledged. The sample size of 30 participants, while powered for the primary outcome based on an assumed effect size, might be insufficient to detect smaller but potentially clinically relevant differences in all secondary micronutrient outcomes. The study was conducted at a single center, which may limit the generalizability of the findings. Furthermore, this study assessed the acute effects of a single HFR and HDF session on micronutrient concentrations; the long-term impacts of sustained HFR or HDF therapy on overall micronutrient status and clinical outcomes were not evaluated. A key limitation is that detailed dietary assessments (e.g., food diaries) were not performed, and thus we could not control for the influence of dietary intake on pre-dialysis micronutrient concentrations. Finally, while the Suprasorb cartridge's general properties are known, its precise adsorptive profile for all measured micronutrients is not fully elucidated.

4.5. Implications for future study

The findings of this study open several avenues for future research. Larger, multicenter, long-term randomized controlled trials are needed to confirm these acute findings and to evaluate the chronic effects of HFR versus HDF on micronutrient status, bone mineral parameters, inflammatory markers, and ultimately, hard clinical outcomes. Future studies should also incorporate detailed dietary assessments.

Further mechanistic studies are warranted to better understand the interactions between specific micronutrients (especially Ca, Vitamin D, Se) and the HFR adsorbent cartridge. This could involve in vitro studies or more detailed kinetic modeling during HFR sessions. Investigating whether different adsorbent materials or operational parameters in HFR could optimize both toxin removal and micronutrient preservation would also be valuable. Research into tailored supplementation strategies for patients on HFR, if the observed decreases in certain nutrients are confirmed to have long-term clinical relevance, would be beneficial. Finally, exploring the clinical impact of better vitamin B3 preservation with HFR could be a focus.

5. Conclusions

In this randomized crossover trial, HFR and HDF showed no significant difference in their acute impact on post-treatment serum iodine concentrations. However, HFR was associated with significantly greater session decreases in serum calcium, vitamin D3, and selenium compared to HDF. Conversely, HFR resulted in significantly higher post-treatment serum concentrations of vitamin B3. For many other micronutrients, the two modalities had comparable effects. These findings suggest that until long-term studies can demonstrate a clear net clinical benefit, the routine implementation of HFR outside of dedicated research contexts appears premature and requires significant caution.

Ethics approval and consent to participate

The study proposal was approved by the institutional review committee of the Naval Medical Center of PLA (registration number: 2024123104). The study was conducted in accordance with the local legislation and institutional requirements. All participants provided written consent.

Consent for publication

Not applicable.

Availability of data and materials

De-identified individual participant data that underlie the results reported in this article will be available from the corresponding author upon reasonable request.

Authors' contributions

NL, and BY designed the study together. CZ led the application for ethics approval and consent. DY, QS, BY, FZ, and CZ are the study clinicians involved in patient care and data collection. BY, ZC, and CX performed data analyses. All authors participated in critically appraising and revising the intellectual content of the manuscript. All authors read and approved the final manuscript. No one eligible for authorship has been excluded from the list of authors.

Declaration of generative AI and AI-assisted technologies in the writing process

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Conflict of interest

The authors declare no competing interests.

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References

[1] Tonelli M, Wiebe N, Knoll G, Bello A, Browne S, Jadhav D, et al. Systematic review: Kidney transplantation compared with dialysis in clinically relevant outcomes. Am J Transplant 2011;11:2093–109. https://doi.org/10.1111/j.1600-6143.2011.03686.x.

[2] Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004;351:1296–305. https://doi.org/10.1056/NEJMoa041031.

[3] Dialysis: a field moving forward. Nat Rev Nephrol 2020;16:543. https://doi.org/10.1038/s41581-020-00347-6. –543.

[4] Mollahosseini A, Abdelrasoul A, Shoker A. A critical review of recent advances in hemodialysis membranes hemocompatibility and guidelines for future development. Mater Chem Phys 2020;248:122911. https://doi.org/10.1016/j.matchemphys.2020.122911.

[5] Ronco C, Clark WR. Haemodialysis membranes. Nat Rev Nephrol 2018;14:394–410. https://doi.org/10.1038/s41581-018-0002-x.

[6] Meyer TW, Hostetter TH. Uremia. N Engl J Med 2007;357:1316–25. https://doi.org/10.1056/NEJMra071313.

[7] Stegmayr B. Dialysis procedures alter metabolic conditions. Nutrients 2017;9. https://doi.org/10.3390/nu9060548.

[8] Tonelli M, Wiebe N, Hemmelgarn B, Klarenbach S, Field C, Manns B, et al. Trace elements in hemodialysis patients: a systematic review and meta-analysis. BMC Med 2009;7:25. https://doi.org/10.1186/1741-7015-7-25.

[9] Kalantar-Zadeh K, Kopple JD. Trace elements and vitamins in maintenance dialysis patients. Adv Ren Replace Ther 2003;10:170–82. https://doi.org/10.1053/j.arrt.2003.09.002.

[10] Chen C-Y, Chiu C-H, Wu I-W, Hsu H-J, Chen Y-T, Hsu C-K, et al. Micronutrients and renal outcomes: a prospective cohort study. Nutrients 2022;14:3063. https://doi.org/10.3390/nu14153063.

[11] Tallman DA, Latifi E, Kaur D, Sulaheen A, Ikizler TA, Chinna K, et al. Dietary patterns and health outcomes among African American maintenance hemodialysis patients. Nutrients 2020;12:797. https://doi.org/10.3390/nu12030797.

[12] Riccio E, Cataldi M, Minco M, Argentino G, Russo R, Brancaccio S, et al. Evidence that p-Cresol and IL-6 are adsorbed by the HFR cartridge: towards a new strategy to decrease systemic inflammation in dialyzed patients? PLoS One 2014;9:e95811. https://doi.org/10.1371/journal.pone.0095811.

[13] Panichi V, Manca-Rizza G, Paoletti S, Taccola D, Consani C, Filippi C, et al. Effects on inflammatory and nutritional markers of haemodiafiltration with online regeneration of ultrafiltrate (HFR) vs online haemodiafiltration: a cross-over randomized multicentre trial. Nephrol Dial Transplant 2006;21:756–62. https://doi.org/10.1093/ndt/gfi189.

[14] Splendiani G, De Angelis S, Tullio T, Ferranini M, Dessì MR, Pastore A, et al. Selective adsorption of homocysteine using an HFR-ON LINE technique. Artif Organs 2004;28:592–5. https://doi.org/10.1111/j.1525-1594.2004.00053.x.

[15] Borrelli S, Minutolo R, De Nicola L, De Simone E, De Simone W, Zito B, et al. Effect of hemodiafiltration with endogenous reinfusion on overt idiopathic chronic inflammation in maintenance hemodialysis patients: a multicenter longitudinal study. Hemodial Int 2014;18:758–66. https://doi.org/10.1111/hdi.12178.

[16] Zhu C, Ding L, Lan N, Zeng F, Ye D, Wang H, et al. The impact of hemodiafiltration with endogenous reinfusion (HFR) on micronutrient status in patients undergoing maintenance hemodialysis: study protocol of a randomized controlled trial. BMC Nephrol 2025;26:222. https://doi.org/10.1186/s12882-025-04148-6.

[17] Lu R, Fang Y, Wu W, Zeng X, Liu T, Qian Y, et al. Hemodiafiltration with endogenous reinfusion for uremic toxin removal in patients undergoing maintenance hemodialysis: a pilot study. Ren Fail 2024;46:2338929. https://doi.org/10.1080/0886022X.2024.2338929.

[18] Kondrup J, Rasmussen HH, Hamberg O, Stanga Z, Ad Hoc ESPEN Working Group. Nutritional risk screening (NRS 2002): a new method based on an analysis of controlled clinical trials. Clin Nutr 2003;22:321–36. https://doi.org/10.1016/s0261-5614(02)00214-5.

[19] Culleton BF. Clinical practice guidelines for hemodialysis adequacy, update 2006. Am J Kidney Dis 2006;48:S2–90. https://doi.org/10.1053/j.ajkd.2006.03.051.

[20] European Best Practice Guidelines Expert Group on Hemodialysis ERA. Section II. Haemodialysis adequacy. Nephrol Dial Transplant 2002;17(Suppl 7):16–31.

[21] Shinoda T, Hata T, Nakajima K, Yoshimoto H, Niwa A. Time-course of iodine elimination by hemodialysis in patients with renal failure after angiography. Ther Apher 2002;6:437–42. https://doi.org/10.1046/j.1526-0968.2002.00469.x.

[22] Gardner DF, Mars DR, Thomas RG, Bumrungsup C, Misbin RI. Iodine retention and thyroid dysfunction in patients on hemodialysis and continuous ambulatory peritoneal dialysis. Am J Kidney Dis 1986;7:471–6. https://doi.org/10.1016/s0272-6386(86)80187-1.

[23] Ronco C, Bellomo R. Hemoperfusion: technical aspects and state of the art. Crit Care 2022;26:135. https://doi.org/10.1186/s13054-022-04009-w.

[24] Kielstein JT, Schwarz A, Arnavaz A, Sehlberg O, Emrich HM, Fliser D. High-flux hemodialysis–an effective alternative to hemoperfusion in the treatment of carbamazepine intoxication. Clin Nephrol 2002;57:484–6. https://doi.org/10.5414/cnp57484.

[25] Bouillon R, Schuit F, Antonio L, Rastinejad F. Vitamin D binding protein: a historic overview. Front Endocrinol 2020;10. https://doi.org/10.3389/fendo.2019.00910.

[26] Saponaro F, Saba A, Zucchi R. An update on vitamin D metabolism. Int J Mol Sci 2020;21:6573. https://doi.org/10.3390/ijms21186573.

[27] Sivgin S. Apheresis methods in hyperlipidemias. Dyslipidemias in kidney disease. New York, NY: Springer New York; 2014. p. 269–85. https://doi.org/10.1007/978-1-4939-0515-7_15.

[28] Omrani H, Golmohamadi S, Pasdar Y, Jasemi K, Almasi A. Effect of selenium supplementation on lipid profile in hemodialysis patients. J Ren Inj Prev 2016;5:179–82. https://doi.org/10.15171/jrip.2016.38.

[29] Polyakova IV, Osipenko AA, Borovikova LN, Ezhova NM, Pisarev OA, Vlasova EN, et al. Synthesis and properties of polymeric and organo-inorganic amphiphilic sorbents molecularly imprinted with cholesterol. Russ J Appl Chem 2015;88:1617–26. https://doi.org/10.1134/S1070427215100109.

[30] Dou W, Wang J, Yao Z, Xiao W, Huang M, Zhang L. A critical review of hemoperfusion adsorbents: materials, functionalization and matrix structure selection. Mater Adv 2022;3:918–30. https://doi.org/10.1039/D1MA00892G.

[31] Khrulev AE, Baykina AN, Shiyanova NA, Ayu Sirotkina, Oyu Salokhina, Grigorieva VN. Status of water-soluble vitamins and neurological disorders in dialysis patients. Neurology Bulletin 2020;LII:55–9. https://doi.org/10.17816/nb17771.

[32] Jankowska M, Lichodziejewska-Niemierko M, Rutkowski B, Dębska-Ślizień A, Małgorzewicz S. Water soluble vitamins and peritoneal dialysis – state of the art. Clinical Nutrition 2017;36:1483–9. https://doi.org/10.1016/j.clnu.2016.12.021.

[33] Hryciuk M, Heleniak Z, Małgorzewicz S, Kowalski K, Antosiewicz J, Koelmer A, et al. Assessment of vitamin D metabolism disorders in hemodialysis patients. Nutrients 2025;17:774. https://doi.org/10.3390/nu17050774.

[34] Bansal B, Bansal S, Mithal A, Kher V, Marwaha R. Vitamin D deficiency in hemodialysis patients. Indian J Endocrinol Metab 2012;16:270. https://doi.org/10.4103/2230-8210.93749.

[35] Mohamadi Najafabadi A, Ahmadi A, Mardani S. Effect of niacin on phosphorus, calcium, parathormone and vitamin D levels in hemodialysis patients; a double-blinded randomized clinical trial. J Nephropharmacol 2022;12:e10569. https://doi.org/10.34172/npj.2022.10569.

[36] Touraine C, Cuer B, Conroy T, Juzyna B, Gourgou S, Mollevi C. When a joint model should be preferred over a linear mixed model for analysis of longitudinal health-related quality of life data in cancer clinical trials. BMC Med Res Methodol 2023;23:36. https://doi.org/10.1186/s12874-023-01846-3.

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