J Appl Biomed
DOI: 10.32725/jab.2024.027
journal homepage: http://jab.zsf.jcu.cz

Journal of Applied Biomedicine

Original research article

Effects of different hemodialysis modalities combined with low-calcium dialysate on mineral metabolism and vascular calcification in maintenance hemodialysis patients with chronic kidney disease

Jing Wang [1], Yimian Luo [2], Xingyu Ji [2], Hao Xu [2], Zhenhua Liang [2], Minjie Zhou [3] *

[1] *Southern Medical University, Nanfang Hospital, Blood Purification Unit, Guangzhou 510515, Guangdong China*
[2] *Southern Medical University, Guangzhou 510515, Guangdong, China*
[3] *Southern Medical University, Nanfang Hospital, Department of Organ Transplantation, Guangzhou 510515, Guangdong, China*

Abstract
Objective: This research investigated the effects of different hemodialysis modalities combined with low-calcium dialysate (LCD) on mineral metabolism and vascular calcification (VC) in maintenance hemodialysis (MHD) patients with chronic kidney disease (CKD).
Methods: General data were collected from 192 cases of MHD patients, who were divided into 4 groups according to the randomized numerical table. Each group was given LCD treatment, and conventional hemodialysis (HD), high-flux HD (HFHD), hemodiafiltration (HDF), and HD + hemoperfusion (HP) were performed, respectively. The patients were dialyzed 3 times per week for 4 h each time, and each group was treated for 6 months. Fasting venous blood was collected. Serum interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and high-sensitive C-reactive protein (hs-CRP) levels were measured by ELISA, calcium (Ca^{2+}), phosphorus (P), Ca^{2+}-P product, serum creatinine (SCr), blood urea nitrogen (BUN), β2 microglobulin (β2-MG), and intact parathyroid hormone (iPTH) were measured by chemiluminescence immunoassay, serum alkaline phosphatase (ALP) was determined by turbidimetric assay, and 25-hydroxyvitamin D (25(OH)D) was measured by autoradiographic immunoassay. To assess the extent of calcification in the iliac artery and abdominal aorta, a multilayer spiral CT device was employed for abdominal scans.
Results: Serum IL-6, hs-CRP, TNF-α, Ca^{2+}, P, Ca^{2+}-P product, SCr, BUN, β2-MG, iPTH, and ALP levels decreased, while 25(OH)D levels increased in the four groups after treatment. The most pronounced effect on the reduction of IL-6, hs-CRP, TNF-α, Ca^{2+}, P, Ca^{2+}-P product, SCr, BUN, β2-MG, iPTH, and ALP was in the HD + HP group, followed by the HDF and HFHD groups, and then by the HD group. The rate of VC in the HDF, HFHD, and HD + HP groups was lower than that in the HD group, and the rate in the HD + HP group was lower than that in the HDF and HFHD groups.
Conclusion: The combination of HD + HP and LCD in treating CKD with MHD is effective, evidently rectifying disruptions in serum Ca^{2+} and P metabolism, enhancing kidney function, lessening the body's inflammatory response, and lessening VC.

Keywords: Calcium and phosphorus metabolism; Hemodiafiltration; Hemofiltration; Hemoperfusion; High-flux hemodialysis; Low-calcium dialysate; Maintenance hemodialysis; Vascular calcification

Highlights:
- HD + HP can effectively reduce IL-6, TNF-α, and hs-CRP in CKD patients with MHD.
- HD + HP reduces Ca^{2+}, P, and Ca^{2+}-P product in CKD patients with MHD.
- HD + HP reduces iPTH and ALP, and increases 25(OH)D in CKD patients with MHD.
- HHD + HP reduces SCr, BUN, and β2-MG levels in CKD patients with MHD.
- HD + HP reduces the degree of vascular calcification in CKD patients with MHD.

Introduction

Chronic kidney disease (CKD) is characterized by prolonged damage to kidney tissue, resulting in an ongoing decline in kidney function, which can slowly advance to end-stage renal disease (ESRD) (Charles and Ferris, 2020). The designation of CKD recognizes that this ailment spans a spectrum with varying levels of kidney dysfunction, as opposed to being a singular instance of renal damage (Akchurin, 2019). Initial stages of CKD show no symptoms, manifesting only in later phases when the disease leads to complications, like reduced

* **Corresponding author:** Minjie Zhou, Southern Medical University, Nanfang Hospital, Department of Organ Transplantation, 1838 Guangzhou North Road, Guangzhou 510515, Guangdong, China; e-mail: Zhouminjie6475@163.com
http://doi.org/10.32725/jab.2024.027
Submitted: 2024-04-12 • Accepted: 2024-12-13 • Prepublished online: 2024-12-16
J Appl Biomed 22/4: 228–233 • EISSN 1214-0287 • ISSN 1214-021X

kidney function and additional related comorbidities. In the later phases, with severely compromised kidney function, treatment options are limited to either dialysis or a transplant (Evans et al., 2022). Hemodialysis (HD) is not only appropriate for the majority of nephropathy patients, but it also serves as an interim therapy for kidney transplants (Shardlow et al., 2017).

The evolution and enhancement of HD methods have led to the emergence of four primary hemodialysis techniques: hemofiltration (HF), hemodiafiltration (HDF), low-flux HD, and high-flux HD (HFHD). HD primarily serves as a treatment for both acute and chronic kidney failure resistant to traditional medical treatments (Alam et al., 2019). It has been suggested that increasing the frequency and length of HD sessions may lead to improved phosphorus (P) control without major effects on calcium (Ca^{2+}) (Daugirdas et al., 2012). Compared with low-flux HD, HFHD can effectively remove intermediate molecular uremic toxins weighing 5000-15,000 Da, improving the prognosis for patients with end-stage renal disease (Liu et al., 2020). HDF merges HF with HD within a singular method. HDF enables the integration of a specified convective dialysis dosage with the standard urea dialysis dosage (Fischbach et al., 2012). HDF combines solute removal via diffusion and convection, purifying more than 20% of the treated blood volume with a high-flux hemodialyzer, and maintaining fluid balance by directly administering sterile, nonpyrogenic replacement fluid into the patient's blood (Canaud et al., 2018). Hemoperfusion (HP) can eliminate the accumulation of protein-bound uremic toxins and mesomolecular toxins in maintenance HD patients and reduce complications (Magnani and Atti, 2021). Considering the different effects of HD methods on CKD, this study mainly focused on the specific effect of these approaches on Ca^{2+} and P metabolism and vascular calcification (VC) in CKD patients.

Materials and methods

Ethics statement

The study complied with the review and approval of the medical ethics committee of our hospital. Written informed consent was acquired from all study subjects.

Subjects

In total, 192 maintenance hemodialysis (MHD) patients admitted to our hospital from January 2019 to December 2021 were divided into an HD group, HFHD group, HDF group, and HD + HP group according to the numerical table method, with 48 cases in each group.

Inclusion criteria: (1) patients who had been on regular HD for more than 12 months (4–5 h each time, 3 times/week); (2) Patients aged 20–75 years old; (3) Patients demonstrating adherence to treatment; (4) Patients with complete clinical data.

Exclusion criteria: (1) those who have had infectious diseases or active immune diseases in the last 3 months; (2) those who have been treated with immunosuppressive drugs in the last 1 month; (3) those with serious primary diseases such as cardiovascular, hepatic, and hematopoietic systems; (4) those with a history of parathyroid or adrenal gland surgery; (5) those with severe malnutrition or malignant tumors.

HD methods

HD group: Treatment was performed with a low-flux polysulfone membrane dialyzer (Diacap LOPS15, Beltron, Germany) with a blood flow of 230–290 ml/min and a dialysate flow of 500 ml/min.

HFHD group: HFHD instrument (Fresenius AG, Germany; model: F60) was used for treatment, with the dialysis flow rate set at 500–800 ml/min, the blood flow rate at 200–300 ml/min, the effective area at 1.4 m^2, and the ultrafiltration coefficient at 46 ml/(h-mmHg) (1 mmHg = 0.133 kPa).

HDF group: HDF treatment was given using a disposable hemofilter (F60S, Fresenius, Germany). Replacement solution was generated online by an HD machine (AK200 ULTRA S, Kimball, Sweden). The blood flow was 230–290 ml/min, dialysate flow rate was 500 ml/min, and total amount of replacement solution was 21.6 l.

HD + HP group: once-a-week HD + HP treatment was performed based on the HD group. The perfusion apparatus was Neutral Macroporous Adsorption Resin (HA-130, Zhuhai Jianfan Construction Labor Service Co., Ltd., China), and the blood flow was 180 ml/min for 2 h. At the end of the perfusion, the blood flow was increased to 220–290 ml/min, and then regular HD was performed for 2 h.

In the four groups, low-calcium dialysate (LCD) treatment was performed (1.25 mmol/l), and MHD was performed for 4 h/times, 3 times/week. All four groups were treated continuously for 6 months.

Observation indices

Venous blood (5 ml) was collected from patients on the day of enrolment (before dialysis treatment) and 6 months after treatment (4–6 h after the end of dialysis treatment). Serum was separated by centrifugation at 3000 r/min for 5 min, with a centrifugation radius of 5 cm, and stored at a low temperature.

Inflammatory factors: Enzyme-linked immunosorbent assay (kit produced by Nanjing Jiancheng Bioengineering Institute, Nanjing, China) was conducted to detect changes in serum interleukin-6 (IL-6), tumor necrosis factor-α (TNF-α), and high-sensitive C-reactive protein (hs-CRP).

Ca^{2+}-P metabolism: Ca^{2+}, P, and Ca^{2+}-P product were measured by chemiluminescence (Hitachi, Japan).

Renal function: Changes in serum creatinine (SCr) and urea nitrogen (BUN) were measured by chemoluminescence homogeneous assay method (Abbott, USA), and β2-microglobulin (β2-MG) levels were measured by electrochemiluminescent assay (Abbott).

Serological indices: Intact parathyroid hormone (iPTH) was determined by chemiluminescence, serum alkaline phosphatase (ALP) by turbidimetric assay, and 25 hydroxyvitamin D [25(OH)D] by automated radioimmunoassay.

VC: Abdominal scanning was performed with SOMATOM Spirit multilayer spiral CT machine, and calcification of the iliac arteries and abdominal aorta was evaluated. A large number of intact arterial calcifications are grade V; calcification involving areas >50% of the arterial diameter is grade IV; calcification involving areas >50% of the arterial diameter is grade III; calcification involving areas ≤50% of the arterial diameter is grade II; calcification areas ≤50% of the arterial diameter is grade I; and absence of calcification is grade 0.

Statistical analysis

SPSS20.0 statistical software was applied to analyze the data, and the enumeration data were expressed as cases (%) and evaluated via χ^2 test or Fisher's exact test. Measurement data were shown as ($\bar{x} \pm s$) and evaluated via *t*-test or analysis of variance. $P < 0.05$ was used to indicate that the difference was statistically significant.

Results

Baseline data

Comparison of baseline data of age, gender, BMI, course of dialysis, and primary diseases in the four groups showed no differences ($P > 0.05$, Table 1).

Serum inflammatory factor levels

Serum IL-6, hs-CRP, and TNF-α levels of the four groups decreased after treatment ($P < 0.05$). Before treatment, the variances in serum IL-6, hs-CRP, and TNF-α concentrations among the four groups lacked statistical significance ($P > 0.05$). Post-treatment, there was a notable reduction in IL-6, hs-CRP, and TNF-α levels in the HDF, HFHD, and HD + HP groups, in comparison to the HD group ($P < 0.05$). The levels of IL-6, hs-CRP, and TNF-α were notably reduced in the HD + HP group when compared with the HDF and HFHD groups ($P < 0.05$, Table 2).

Serum Ca^{2+} and P

Ca^{2+}, P, and Ca^{2+}-P product of the four groups decreased after treatment ($P < 0.05$). The difference between the four groups in Ca^{2+}, P, and Ca^{2+}-P product was not statistically significant before treatment ($P > 0.05$). HDF, HFHD, and HD + HP groups showed significantly lower levels of Ca^{2+}, P, and Ca^{2+}-P product than those of the HD group ($P < 0.05$). It was significant that the Ca^{2+}, P, and Ca^{2+}-P product of the HD + HP group were lower than those of the HDF group and the HFHD group ($P < 0.05$, Table 3).

Table 1. Comparison of baseline data of four groups of patients

Indicators	HD group ($n = 48$)	HFHD group ($n = 48$)	HDF group ($n = 48$)	HD + HP group ($n = 48$)	P value
Age (years)	46.59 ± 7.33	45.45 ± 7.02	46.03 ± 7.18	44.89 ± 7.45	0.688
Gender					0.739
Male	30	27	29	25	
Female	18	21	19	23	
Body mass index (kg/m^2)	21.29 ± 3.26	21.40 ± 3.39	22.45 ± 3.97	22.37 ± 3.43	0.223
Duration of dialysis (months)	31.44 ± 2.54	31.21 ± 2.19	32.50 ± 2.83	31.55 ± 2.75	0.078
Primary diseases					0.999
Chronic glomerulonephritis	22	22	25	22	
Diabetic nephropathy	13	14	11	12	
Hypertensive kidney damage	8	7	8	8	
Others	5	5	4	6	

Table 2. Comparison of serum inflammatory factor levels before and after treatment in four groups of patients

Groups	IL-6 (pg/ml)		hs-CRP (mg/l)		TNF-α (pg/ml)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
HD group ($n = 48$)	150.69 ± 15.72	134.23 ± 13.57*	15.22 ± 1.87	13.40 ± 1.49*	186.68 ± 18.70	168.35 ± 17.58*
HFHD group ($n = 48$)	151.66 ± 15.35	121.85 ± 12.87*#	14.75 ± 1.82	11.47 ± 1.33*#	185.10 ± 18.17	152.39 ± 14.91*#
HDF group ($n = 48$)	152.65 ± 16.12	122.56 ± 12.37*#	14.99 ± 1.64	11.65 ± 1.45*#	186.79 ± 18.22	150.04 ± 13.21*#
HD + HP group ($n = 48$)	150.44 ± 15.78	110.71 ± 10.81*#$&	14.86 ± 1.90	9.34 ± 1.06*#$&	188.48 ± 18.79	122.89 ± 11.12*#$&

Note: * indicates $P < 0.05$ compared with before treatment; # indicates $P < 0.05$ compared with HD group; $ indicates $P < 0.05$ compared with HFHD group; & indicates $P < 0.05$ compared with HDF group. HD, hemodialysis; HFHD, high-flux hemodialysis; HDF, hemodiafiltration; HP, hemoperfusion; IL-6, interleukin-6; hs-CRP, high-sensitive C-reactive protein; TNF-α, tumor necrosis factor-α.

Table 3. Comparison of serum calcium and phosphorus levels before and after treatment in four groups

Groups	Calcium (mmol/l)		Phosphorus (mmol/l)		Calcium-phosphorus product (mg^2/dl)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
HD group ($n = 48$)	2.51 ± 0.31	2.23 ± 0.22*	2.68 ± 0.29	1.99 ± 0.25*	78.48 ± 5.85	54.14 ± 5.28*
HFHD group ($n = 48$)	2.55 ± 0.32	2.08 ± 0.17*#	2.61 ± 0.25	1.55 ± 0.19*#	78.73 ± 5.22	44.83 ± 4.33*#
HDF group ($n = 48$)	2.58 ± 0.30	2.13 ± 0.18*#	2.66 ± 0.23	1.53 ± 0.20*#	76.20 ± 5.36	44.41 ± 4.52*#
HD + HP group ($n = 48$)	2.57 ± 0.36	1.85 ± 0.13*#$&	2.63 ± 0.24	1.13 ± 0.15*#$&	77.98 ± 5.34	40.59 ± 4.10*#$&

Note: * indicates $P < 0.05$ compared with before treatment; # indicates $P < 0.05$ compared with HD group; $ indicates $P < 0.05$ compared with HFHD group; & indicates $P < 0.05$ compared with HDF group. HD, hemodialysis; HFHD, high-flux hemodialysis; HDF, hemodiafiltration; HP, hemoperfusion.

Renal function

Serum SCr, BUN, and β2-MG levels of the four groups decreased after treatment, and the differences were statistically significant when compared with those before treatment ($P < 0.05$). Before treatment, the differences between the four groups were not statistically significant when compared with the four groups ($P > 0.05$). After treatment, SCr, BUN, and β2-MG levels of the HDF group, HFHD group, and HD + HP group were lower than those of the HD group ($P < 0.05$). SCr, BUN, and β2-MG levels in the HD + HP group were lower than those in the HDF group and HFHD group ($P < 0.05$, Table 4).

Serologic indices

Serum iPTH and ALP levels decreased and 25(OH)D levels increased in all four groups after treatment ($P < 0.05$). A comparison of serum iPTH, ALP, and 25(OH)D between the four groups revealed no statistically significant differences before treatment ($P > 0.05$). As a result of treatment, the HDF, HD + HP, and HDF + ALP groups had lower levels of iPTH and ALP as well as higher levels of 25(OH)D than the HD group ($P < 0.05$). As compared to the HDF and HFHD groups, the HD + HP group had lower iPTH and ALP levels, and the 25(OH)D level was significantly higher ($P < 0.05$, Table 5).

VC grading

VC rate of the HDF group, HFHD group, and HD + HP group was lower than that of the HD group, and the VC rate of the HD + HP group was lower than that of the HDF group and HFHD group ($P < 0.05$, Table 6).

Table 4. Comparison of renal function before and after treatment in four groups

Groups	SCr (μmol/l)		BUN (mmol/l)		β2-MG (mg/l)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
HD group (n = 48)	995.69 ± 124.32	496.07 ± 71.13*	37.33 ± 6.54	15.41 ± 2.87*	36.07 ± 5.15	28.77 ± 5.64*
HFHD group (n = 48)	993.91 ± 134.03	465.02 ± 66.55*#	39.83 ± 6.31	12.39 ± 2.14*#	37.32 ± 5.09	25.50 ± 4.15*#
HDF group (n = 48)	991.86 ± 129.83	459.07 ± 59.75*#	38.76 ± 6.86	12.33 ± 2.29*#	36.17 ± 5.85	24.39 ± 4.62*#
HD + HP group (n = 48)	976.38 ± 132.74	402.63 ± 55.84*#$&	38.13 ± 6.75	10.47 ± 1.74*#$&	35.38 ± 5.94	21.91 ± 3.36*#$&

Note: * indicates $P < 0.05$ compared with before treatment; # indicates $P < 0.05$ compared with HD group; $ indicates $P < 0.05$ compared with HFHD group; & indicates $P < 0.05$ compared with HDF group. HD, hemodialysis; HFHD, high-flux hemodialysis; HDF, hemodiafiltration; HP, hemoperfusion; SCr, serum creatinine; BUN, blood urea nitrogen; β2-MG, β2 microglobulin.

Table 5. Comparison of serologic indices before and after treatment in four groups

Groups	iPTH (pg/ml)		ALP (U/L)		25(OH)D (ng/ml)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
HD group (n = 48)	690.80 ± 84.23	539.25 ± 67.72*	138.16 ± 16.56	113.13 ± 14.25*	14.14 ± 2.56	16.15 ± 3.47*
HFHD group (n = 48)	683.45 ± 83.16	446.82 ± 56.89*#	135.56 ± 17.27*	100.33 ± 14.49*#	14.22 ± 2.33	20.28 ± 3.90*#
HDF group (n = 48)	681.88 ± 84.51	454.49 ± 55.64*#	136.95 ± 18.72	98.70 ± 14.14*#	14.49 ± 2.25	20.45 ± 3.88*#
HD + HP group (n = 48)	687.24 ± 89.43	361.24 ± 40.22*#$&	137.43 ± 17.56	85.81 ± 13.83*#$&	14.26 ± 2.37	22.89 ± 4.09*#$&

Note: * indicates $P < 0.05$ compared with before treatment; # indicates $P < 0.05$ compared with HD group; $ indicates $P < 0.05$ compared with HFHD group; & indicates $P < 0.05$ compared with HDF group. HD, hemodialysis; HFHD, high-flux hemodialysis; HDF, hemodiafiltration; HP, hemoperfusion; iPTH, intact parathyroid hormone; ALP, alkaline phosphatase; 25(OH)D, 25-hydroxyvitamin D.

Table 6. Comparison of the grading of calcification between the two groups [*n* (%)]

Groups	Grade 0	Grade I	Grade II	Grade III	Grade IV	Grade V	Calcification rate
HD group (n = 48)	1 (2.08)	14 (29.17)	12 (25.00)	11 (6.25)	7 (14.58)	3 (6.25)	47 (97.92)
HFHD group (n = 48)	8 (16.67)	11 (22.92)	12 (25.00)	10 (20.83)	4 (8.33)	3 (6.25)	40 (83.33)*
HDF group (n = 48)	9 (18.75)	10 (20.83)	12 (25.00)	10 (20.83)	3 (6.25)	4 (8.33)	39 (81.25)*
HD + HP group (n = 48)	19 (39.58)	8 (16.67)	8 (16.67)	7 (14.58)	4 (8.33)	2 (4.17)	29 (60.42)*#$

Note: * indicates $P < 0.05$ compared with HD group; # indicates $P < 0.05$ compared with HFHD group; $ indicates $P < 0.05$ compared with HDF group. HD, hemodialysis; HFHD, high-flux hemodialysis; HDF, hemodiafiltration; HP, hemoperfusion.

Discussion

CKD is a non-reversible event that is linked to an increased risk of cardiovascular issues (Ammirati, 2020). For individuals suffering from renal failure, kidney replacement therapy – either through dialysis or a kidney transplant – serves as a crucial life-preserving therapy (Gondal, 2023). LCD not only aids in preventing and treating VC but also boosts the release of parathyroid hormones and lowers the likelihood of low-transport bone disorders (Wen et al., 2018). Based on LCD, this research mainly focused on four different HD methods to assess their performance on CKD patients.

CKD evolves from a localized inflammatory condition to a widespread inflammatory disease over time (AIRG-E et al., 2022). In patients with CKD, abnormal levels of pro-inflammatory cytokines such as IL-6, hs-CRP, and TNF-α might be linked to the widespread microinflammation in these individuals (Amdur et al., 2016). The current research determined these inflammatory indicators and revealed that HD + HP effectively reduced inflammation in CKD patients when compared with HFHD or HDF. Further, treatment with HD resulted in the least effective anti-inflammatory impact. The combined clinical impact of HD and HP on older MHD patients is substantial, significantly lowering hs-CRP, IL-6, and TNF-α in these patients (Li et al., 2022). Additionally, integrating HD with HP for treating multiple organ dysfunction syndrome patients may markedly enhance biochemical markers and successfully eliminate inflammatory agents including TNF-α and IL-6 (Wang et al., 2016).

Recent advances in metabolomics have uncovered a strong link between CKD and the imbalance of various metabolites, including nucleotides, amino acids, lipids, and glycoses (Wang et al., 2019). Ca^{2+} and P metabolism disturbances are almost always a consequence of CKD (Felsenfeld et al., 2015). It is vital to control the Ca^{2+} and P metabolism in CKD as P and Ca^{2+} accumulation are associated with poor outcomes (Cannata-Andia and Martin, 2016). This research found that Ca^{2+}, P, and Ca^{2+}-P product decreased most significantly in the HD + HP group, followed by the HDF and HFHD groups, and then the HD group. This suggests that HD + HP treatment was the most effective to control Ca^{2+} and P metabolism in CKD patients. HD + HP combined treatment has been suggested to reduce Ca^{2+}-P and P in patients with Ca^{2+}-P metabolism disorder (Li et al., 2023).

In clinical settings, SCr concentration is commonly considered an indicator of renal function (Pan et al., 2014). During the later phases of CKD, a simultaneous rise in BUN levels is observed, with elevated BUN levels linked to poor outcomes (Seki et al., 2019). β2-MG, an indicator of renal function, is a predictor of renal failure and death rates in the broader populace (Stoppini and Bellotti, 2015). The study utilized these trio of metrics to evaluate the renal function of CKD sufferers, verifying that the quartet of HD approaches enhanced renal function in these patients, with HD + HP exhibiting superior effectiveness. Accordingly, a retrospective study has revealed that HD + HP treatment can improve renal function, in part by lowering BUN and SCr in patients with acute renal failure (Wang et al., 2021).

iPTH, ALP, and 25(OH)D are robust bone metabolism markers (Liu and He, 2015). By measuring iPTH, ALP, and 25(OH)D, this research demonstrated that the four HD modalities reduced iPTH and ALP and elevated 25(OH)D, with HD + HP modality showing superior efficacy. VC, characterized by the accumulation of Ca^{2+} phosphate crystals predominantly as hydroxyapatite in blood vessels, is acknowledged as a standalone indicator of vascular health risks and death in CKD (Kanbay et al., 2023). This phenomenon is noticeable in arteries regardless of their size and may occur within the intima and/or the media layer of these vessels (Marreiros et al., 2022). Despite the lack of agreement on particular treatment methods, approaches concentrating on maintaining phosphate equilibrium and regulating Ca^{2+} levels are holding therapeutic promise (Cozzolino et al., 2023). The study revealed a reduction in VC among CKD patients receiving various HD treatments. Compared to the other three methods, the HD + HP group yielded superior results.

Conclusion

This paper reveals that HD + HP, based on LCD therapy for CKD, has the potential to rectify disorders in serum Ca^{2+} and P metabolism, enhance renal function, diminish inflammation and VC, and be advocated for clinical application.

Funding
This work was supported by the President Foundation of Nanfang Hospital, Southern Medical University (No. 2022A029).

Ethical aspects and conflict of interest
The authors have no conflict of interest to declare.

References

AIRG-E, EKPF, ALCER, FRIAT, REDINREN, RICORS2040, et al. (2022). CKD: The burden of disease invisible to research funders. Nefrologia 42(1): 65–84. DOI: 10.1016/j.nefro.2021.09.004.

Akchurin OM (2019). Chronic Kidney Disease and Dietary Measures to Improve Outcomes. Pediatr Clin North Am 66(1): 247–267. DOI: 10.1016/j.pcl.2018.09.007.

Alam MB, Khatoon F, Begum SA, Alam MM, Faraji AH, Mahmud MA, et al. (2019). Assessment of Quality of Life of Chronic Kidney Disease Patients Receiving Hemodialysis with Kidney Disease Quality of Life-36 Scale. Mymensingh Med J 28(4): 906–913.

Amdur RL, Feldman HI, Gupta J, Yang W, Kanetsky P, Shlipak M, Rahman M, et al. (2016). Inflammation and Progression of CKD: The CRIC Study. Clin J Am Soc Nephrol 11(9): 1546–1556. DOI: 10.2215/CJN.13121215.

Ammirati AL (2020). Chronic Kidney Disease. Rev Assoc Med Bras (1992) 66(Suppl. 1): s03–s09. DOI: 10.1590/1806-9282.66.S1.3.

Canaud B, Vienken J, Ash S, Ward RA, Kidney Health Initiative HDF Workgroup (2018). Hemodiafiltration to Address Unmet Medical Needs ESKD Patients. Clin J Am Soc Nephrol 13(9): 1435–1443. DOI: 10.2215/CJN.12631117.

Cannata-Andia JB, Martin KJ (2016). The challenge of controlling phosphorus in chronic kidney disease. Nephrol Dial Transplant 31(4): 541–547. DOI: 10.1093/ndt/gfv055.

Charles C, Ferris AH (2020). Chronic Kidney Disease. Prim Care 47(4): 585–595. DOI: 10.1016/j.pop.2020.08.001.

Cozzolino M, Maffei Faccioli F, Cara A, Boni Brivio G, Rivela F, Ciceri P, et al. (2023). Future treatment of vascular calcification in chronic kidney disease. Expert Opin Pharmacother 24(18): 2041–2057. DOI: 10.1080/14656566.2023.2266381.

Daugirdas JT, Chertow GM, Larive B, Pierratos A, Greene T, Ayus JC, et al. (2012). Effects of frequent hemodialysis on measures of CKD mineral and bone disorder. J Am Soc Nephrol 23(4): 727–738. DOI: 10.1681/ASN.2011070688.

Evans M, Lewis RD, Morgan AR, Whyte MB, Hanif W, Bain SC, et al. (2022). A Narrative Review of Chronic Kidney Disease in Clinical Practice: Current Challenges and Future Perspectives. Adv Ther 39(1): 33–43. DOI: 10.1007/s12325-021-01927-z.

Felsenfeld AJ, Levine BS, Rodriguez M (2015). Pathophysiology of Calcium, Phosphorus, and Magnesium Dysregulation in Chronic Kidney Disease. Semin Dial 28(6): 564–577. DOI: 10.1111/sdi.12411.

Fischbach M, Fothergill H, Zaloszyc A, Seuge L (2012). Hemodiafiltration: the addition of convective flow to hemodialysis. Pediatr Nephrol 27(3): 351–356. DOI: 10.1007/s00467-011-1779-z.

Gondal M (2023). Overview of, and Preparations for, Dialysis. Med Clin North Am 107(4): 681–687. DOI: 10.1016/j.mcna.2023.03.003.

Kanbay M, Copur S, Tanriover C, Yavuz F, Galassi A, Ciceri P, Cozzolino M (2023). The pathophysiology and

management of vascular calcification in chronic kidney disease patients. Expert Rev Cardiovasc Ther 21(2): 75–85. DOI: 10.1080/14779072.2023.2174525.

Li J, Li H, Deng W, Meng L, Gong W, Yao H (2022). The Effect of Combination Use of Hemodialysis and Hemoperfusion on Microinflammation in Elderly Patients with Maintenance Hemodialysis. Blood Purif 51(9): 739–746. DOI: 10.1159/000518857.

Li W, Wang J, Wang Y, Guan R, Zhao F, Zhang R (2023). Additional hemoperfusion for patients receiving maintenance hemodialysis: a retrospective analysis. Am J Transl Res 15(6): 4045–4054.

Liu S, Liu H, Wang Z, Teng L, Dong C, Gui T, Zhang Y (2020). Effect of changing treatment to high-flux hemodialysis (HFHD) on mortality in patients with long-term low flux hemodialysis (LFHD): a propensity score matched cohort study. BMC Nephrol 21(1): 485. DOI: 10.1186/s12882-020-02145-5.

Liu Y, He Q (2015). Alkaline Phosphatase, iPTH and Bone Turnover Markers in Chinese Advanced Chronic Kidney Disease Patients. Clin Lab 61(7): 839–843. DOI: 10.7754/clin.lab.2015.141101.

Magnani S, Atti M (2021). Uremic Toxins and Blood Purification: A Review of Current Evidence and Future Perspectives. Toxins (Basel) 13(4): 246. DOI: 10.3390/toxins13040246.

Marreiros C, Viegas C, Simes D (2022). Targeting a Silent Disease: Vascular Calcification in Chronic Kidney Disease. Int J Mol Sci 23(4): 16114. DOI: 10.3390/ijms232416114.

Pan P, Binjie H, Min L, Lipei F, Yanli N, Junwen Z, Xianghua S (2014). A meta-analysis on diagnostic value of serum cystatin C and creatinine for the evaluation of glomerular filtration function in renal transplant patients. Afr Health Sci 14(4): 1025–1035. DOI: 10.4314/ahs.v14i4.34.

Seki M, Nakayama M, Sakoh T, Yoshitomi R, Fukui A, Katafuchi E, et al. (2019). Blood urea nitrogen is independently associated with renal outcomes in Japanese patients with stage 3-5 chronic kidney disease: a prospective observational study. BMC Nephrol 20(1): 115. DOI: 10.1186/s12882-019-1306-1.

Shardlow A, McIntyre NJ, Fraser SDS, Roderick P, Raftery J, Fluck RJ, et al. (2017). The clinical utility and cost impact of cystatin C measurement in the diagnosis and management of chronic kidney disease: A primary care cohort study. PLoS Med 14(10): e1002400. DOI: 10.1371/journal.pmed.1002400.

Stoppini M, Bellotti V (2015). Systemic amyloidosis: lessons from beta2-microglobulin. J Biol Chem 290(16): 9951–9958. DOI: 10.1074/jbc.R115.639799.

Wang G, Li Z, Zhang Y, Pan Y, Chen L (2021). Comparison of Combined Hemodialysis and Hemoperfusion with Hemoperfusion Alone in 106 Patients with Diabetic Ketoacidosis and Acute Renal Failure: A Retrospective Study from a Single Center in China. Med Sci Monit 27: e922753. DOI: 10.12659/MSM.922753.

Wang YN, Ma SX, Chen YY, Chen L, Liu BL, Liu QQ, Zhao YY (2019). Chronic kidney disease: Biomarker diagnosis to therapeutic targets. Clin Chim Acta 499: 54–63. DOI: 10.1016/j.cca.2019.08.030.

Wang YT, Fu JJ, Li XL, Li YR, Li CF, Zhou CY (2016). Effects of hemodialysis and hemoperfusion on inflammatory factors and nuclear transcription factors in peripheral blood cell of multiple organ dysfunction syndrome. Eur Rev Med Pharmacol Sci 20(4): 745–750.

Wen Y, Gan H, Li Z, Sun X, Xiong Y, Xia Y (2018). Safety of Low-calcium Dialysate and its Effects on Coronary Artery Calcification in Patients Undergoing Maintenance Hemodialysis. Sci Rep 8(1): 5941. DOI: 10.1038/s41598-018-24397-w.