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ARTICLE

Effect of Hemodialysis Combined With Hemodiafiltration on Cardiac Structure, Function, and Metabolic Indicators in Uremic Patients

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Abstract

Aims/Background Uremia is a severe manifestation of end-stage renal failure, with high cardiovascular risk, and current dialysis treatments like hemodialysis (HD) face limitations in toxin clearance, necessitating more effective therapeutic strategies. This study aims to evaluate the clinical efficacy of HD combined with hemodiafiltration (HDF) in treating uremia and its influence on cardiac ultrasound indices.

Methods This study retrospectively analyzed clinical data from 80 uremic patients treated at the Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University between April 2019 and April 2023. Based on different therapeutic regimens, patients were divided into a control group (n = 41) and an observation group (n = 39). The control group received HD, while the observation group underwent HD combined with HDF. The cardiac structure, cardiac function, lipid metabolism, and other biochemical indicators were comparatively assessed between the two groups.

Results There were no significant differences in baseline characteristics between the two groups ($p > 0.05$). Before treatment, both groups demonstrated no significant difference in left atrial diameter (LAD), left ventricular posterior wall thickness (LVPWT), interventricular septal thickness (IVST), left ventricular end-diastolic diameter (LVEDD), brain natriuretic peptide (BNP), and troponin T (TnT) ($p > 0.05$). However, after 6 months of treatment, these indices were significantly declined in the observation group ($p < 0.05$). Similarly, no significant differences were observed in left ventricular ejection fraction (LVEF), fractional shortening (FS), cardiac output (CO), stroke volume (SV), and peak mitral E-wave velocity/peak mitral A-wave velocity (E/A) before treatment ($p > 0.05$). However, a significant improvement was observed in the observation group following 6 months of treatment ($p < 0.05$). Before treatment, there were no significant differences in serum creatinine (Scr), blood urea nitrogen (BUN), β2-microglobulin (β2-MG), and parathyroid hormone (PTH) between the two groups ($p > 0.05$). However, the observation group showed significant improvements in Scr, BUN, β2-MG, and PTH after treatment ($p < 0.001$). Additionally, the two study groups had no significant differences in total cholesterol (TC), triglycerides (TG), and low-density lipoprotein (LDL) before treatment ($p > 0.05$). However, their levels decreased significantly in the observation group after treatment ($p < 0.05$). Hypertension and hypotension occurred less frequently in the observation group ($p < 0.05$), with no significant differences observed in the incidence of arrhythmia and infection between the two groups ($p > 0.05$).

Conclusion HD combined with HDF effectively improves cardiac structure and function, reduces metabolic wastes such as Scr, BUN and β2-MG, and decreases blood lipid levels in uremic patients. This study further confirmed the clinical efficacy of this combined approach in treating uremia, which is of positive significance for the prevention and treatment of cardiovascular diseases in uremic patients.

Key words: hemodialysis; uremia; hemodiafiltration; cardiac function; metabolic

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Introduction

Uremia, also referred to as uremic syndrome, is a clinical manifestation of end-stage renal failure, posing a significant risk to patient health and survival (Meijers et al, 2024). Hemodialysis (HD), a widely used renal replacement therapy, effectively eliminates metabolic waste, regulates water, electrolytes, and acid-base balance, and stabilizes the internal environment, thereby prolonging the survival time of patients. As the primary treatment option for patients with stage 5 chronic kidney disease (CKD) globally, HD plays a pivotal role in managing end-stage renal failure (Zhao et al, 2017).

However, conventional HD has limitations in eliminating middle and high molecular weight toxins, which are associated with increased inflammation, endothelial dysfunction, and cardiovascular complications (Harlacher et al, 2022; Nguyen et al, 2021). These complications significantly contribute to the high mortality rates among HD patients, primarily due to cardiovascular events (Tang et al, 2022). Hemodiafiltration (HDF), an advanced renal replacement therapy, has emerged as a promising alternative intervention, offering enhanced removal of middle and high molecular weight toxins while also reducing inflammation and improving cardiovascular outcomes (Ağbaş et al, 2018; Pedreros-Rosales et al, 2023; Roumeliotis et al, 2021).

Despite the growing adoption of HDF, comprehensive studies evaluating its combined use with HD for improving cardiac function and overall prognosis in uremic patients remain limited. Cardiovascular complications are the leading cause of mortality, emphasizing a critical need for therapeutic strategies to mitigate these risks. Echocardiography, particularly Doppler ultrasound, offers a non-invasive and reliable method for assessing cardiac function and predicting cardiovascular events (Simpson et al, 2019). While previous research has primarily focused on ventricular wall motion in uremic cardiomyopathy, further investigations are needed to assess the broader impacts of combined HD and HDF therapy on cardiac structure and function (Hong et al, 2022).

This study addresses this gap by retrospectively evaluating the clinical efficacy of combining HD with HDF in treating uremia and its effects on cardiac ultrasound indices, lipid metabolism, and other metabolic markers. The findings provide novel insights into the potential of combined HD and HDF therapy as an effective therapeutic regimen for improving cardiovascular outcomes and optimizing the overall management of uremic patients.

Methods

Inclusion and Exclusion Criteria

Inclusion criteria included (1) patients aged 18 years or above, (2) those with normal consciousness, (3) patients with complete medical records and follow-up data, (4) HD duration of at least 3 months, and (5) patients with no history of lipid-lowering medications (e.g., statins, ezetimibe), hormonal drugs, or other medications potentially affecting lipid metabolism within the past 6 months.

However, individuals meeting the following criteria were excluded from the study cohort: (1) patients with congenital heart disease, non-renal heart disease, primary hypertension, and valvular heart disease; (2) patients with malignant tumors; (3) patients with severe liver diseases (e.g., cirrhosis, fatty liver) or respiratory diseases (e.g., chronic obstructive pulmonary disease).

Sample Size Calculation

The sample size was determined using an established formula, with β2-microglobulin (β2-MG) as the primary outcome (Nistor et al, 2015; Ward et al, 2000).

$$n = \frac{2 \times \left(Z_{\alpha/2} + Z_{\beta}\right)^2 \times (\sigma)^2}{\Delta^2}$$

$\sigma = 0.05$; $\beta = 0.80$; $Z_{\alpha/2} = 1.96$; $Z_{\beta} = 0.84$.

Based on Ward's study, the mean and standard deviation for the two groups were 61 $\pm$ 4.89 and 38 $\pm$ 4.58, respectively. Therefore, the pooled standard deviation (σ) was determined as 4.74, with $\Delta = 3.79$. This analysis yielded an estimated sample size of approximately 24.5 per group. Based on this calculation, the required sample size for each group was about 25, indicating that the sample size included in this study was sufficient.

Study Design and Procedures

Grouping Methods

This study retrospectively analyzed the clinical data of 85 uremic patients treated at the Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University between April 2019 and April 2023. Five patients were excluded, including three cases with incomplete clinical data, one with congenital heart disease, and one with malignant tumor, resulting in a final study cohort of 80 cases. Based on the therapeutic regimens, the patients were divided into the control group (n = 41) and the observation group (n = 39). The observation group underwent a combination of HD and HDF, and the control group received only HD.

Patient Treatment Protocols

The control group received HD employing a hemodialysis machine (4008S, Fresenius, Bart Humboldt, Hessen, Germany) for 4 hours per session, three times a week, over a continuous period of 6 months. Before dialysis, 1000 mL of 0.9% sodium chloride injection (Specification: 500 mL:4.5 g; National Medical Products Administration (NMPA) No.: H33021575; Batch No.: A2405031; Hangzhou Minsheng Pharmaceutical Co., Ltd., Hangzhou, Zhejiang, China) was used to flush the pipeline and remove air, with the pump speed of 200–250 mL/min.

The observation group received HDF using a hemofiltration machine (5008S, Fresenius, Bart Humboldt, Hessen, Germany). Continuous HDF was performed through internal arteriovenous fistula puncture or internal jugular vein puncture. The replacement fluid rate was set at 3500–4500 mL/h, and the blood flow was 200–300 mL/min. Furthermore, each session was performed once a week for 4 hours on the same day as one of the dialysis sessions.

Doppler Ultrasound Examination

All patients were examined using a Philips Doppler echocardiography machine (EPIQ7C, Royal Dutch Philips Electronics Ltd., Amsterdam, the Netherlands) before and 6 months after treatment, employing a probe frequency of 2.0–5.5 MHz. During the examination, patients were positioned in the left lateral position. Essential indicators such as left atrial diameter (LAD), left ventricular posterior wall thickness (LVPWT), interventricular septal thickness (IVST), left ventricular end-diastolic diameter (LVEDD), left ventricular ejection fraction (LVEF), fractional shortening (FS), cardiac output (CO), and stroke volume (SV) were assessed using the S5-1 ultrasound probe (Royal Dutch Philips Electronics Ltd., Amsterdam, the Netherlands). From the apical four-chamber view, the Doppler sample volume was positioned at the mitral valve to determine peak mitral E-wave velocity (E) and peak mitral A-wave velocity (A), followed by calculating the peak mitral E-wave velocity/peak mitral A-wave velocity (E/A) ratio. To ensure reliability, each measurement was recorded over 3 cardiac cycles, with the mean value used as the final result.

Doppler ultrasound results were recorded as follows:

Left atrial enlargement: LAD $>$35 mm; interventricular septum thickening: IVST $>$12 mm; decreased left ventricular systolic function: LVEF $<$50%; left ventricular posterior wall thickening: LVPWT $>$12 mm (Lancellotti et al, 2013).

Data Collection

Baseline Information

The collected baseline characteristics of patients included age, sex, body mass index, underlying diseases, HD duration, vascular access, and disease duration.

Cardiac Structure and Function Indices

The left ventricular structural indices, including LAD, LVPWT, IVST, and LVEDD, were documented for all patients before and 6 months after treatment.

Similarly, the cardiac systolic function indices, including LVEF, FS, CO, SV, and E/A ratio, were recorded before and 6 months after treatment.

Brain Natriuretic Peptide and Cardiac Troponin T

Blood samples (5 mL) were collected from each patient before treatment and 6 months after treatment to measure brain natriuretic peptide (BNP) and high-sensitivity cardiac troponin T (hsTnT). BNP levels were assessed using chemiluminescent immunoassay (CLIA) through the Roche Elecsys 2010 immunoassay analyzer (Roche Diagnostics GmbH, Mannheim, Germany) and the Roche Elecsys ProBNP reagent kit (Catalog Number: 09315284190, Roche Diagnostics GmbH, Mannheim, Germany). HsTnT levels were measured using high-sensitivity enzyme-linked immunosorbent assay (hs-ELISA) through the Roche Cobas e601 immunoassay analyzer (Roche Diagnostics GmbH, Mannheim, Germany) and the Roche Cobas hsTnT reagent kit (Catalog No.09315357190, Roche Diagnostics GmbH, Mannheim, Germany).

Serum Biochemical Indices

The serum biochemical parameters, including serum creatinine (Scr), blood urea nitrogen (BUN), β2-microglobulin (β2-MG), and parathyroid hormone (PTH), were assessed for all patients before treatment (pre-dialysis) and 6 months after treatment (post-dialysis). In the morning, 5 mL of fasting venous blood was collected from each patient and analyzed using an automatic biochemical analyzer (AU5800, Beckman Coulter, Inc., Brea, CA, USA).

Lipid Metabolism Indices

The lipid metabolism indicators, including total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL), were assessed for each patient before treatment and 6 months after treatment. In the morning, 2 mL of fasting venous blood was obtained from each patient and analyzed using an automatic biochemical analyzer (AU5800, Beckman Coulter, Inc., Brea, CA, USA).

Complication Assessment

Each patient was assessed for the incidence of hypertension, hypotension, arrhythmia, angina, and infections during dialysis.

Table 1. Comparison of baseline characteristics between the two groups ($(\bar{x} \pm s)$/n (%)).

Items		Control group (n = 41)	Observation group (n = 39)	t/χ^2	*p*-value
Age (years)		62.37 ± 7.15	63.41 ± 6.49	0.683	0.497
Body mass index (kg/m^2)		20.09 ± 0.68	20.35 ± 0.66	1.744	0.085
Sex	Male	26 (63.41)	24 (61.54)	0.030	0.862
	Female	15 (36.59)	15 (38.46)		
Disease duration (years)		3.51 ± 1.86	3.21 ± 1.92	0.726	0.470
HD duration (months)		17.10 ± 7.99	16.67 ± 6.50	0.264	0.793
Underlying diseases	Chronic glomerulonephritis	11 (26.83)	9 (23.08)	0.555	0.968
	Diabetic nephropathy	7 (17.07)	8 (20.52)		
	Chronic pyelonephritis	9 (21.95)	10 (25.64)		
	Polycystic kidney disease	8 (19.51)	6 (15.38)		
	Lupus nephritis	6 (14.64)	6 (15.38)		
Vascular access	Arteriovenous fistula	36 (87.80)	33 (84.62)	0.171	0.679
	Central catheterization	5 (12.20)	6 (15.38)		

HD, hemodialysis.

Statistical Analysis

The data were statistically analyzed using SPSS 26.0 (IBM Corp., Armonk, NY, USA). Categorical variables were expressed as (n (%)) and analyzed using the Chi-square or Fisher exact tests. Continuous variables were tested for normality using the Shapiro-Wilk method. The data following a normal distribution were presented as mean ± standard deviation and analyzed using a *t*-test. However, non-normally

distributed variables were expressed as median (P_{25}, P_{75}), and analyzed using the Mann-Whitney U test. The significance level was set at a p-value of <0.05.

Results

Comparison of Baseline Characteristics Between the Two Groups

The two study groups had no significant differences in baseline characteristics, such as age, body mass index, sex, disease duration, HD duration, underlying diseases, and vascular access ($p > 0.05$, Table 1).

Comparison of Cardiac Structure Indices Between the Two Groups

Before treatment, the results for LAD, LVPWT, IVST, and LVEDD were similar between the two groups ($p > 0.05$). After 6 months of treatment, the observation group demonstrated a significant decrease in LAD, LVPWT, IVST, and LVEDD ($p < 0.001$, Table 2).

Table 2. Comparison of cardiac structure indices between the two groups (($\bar{x} \pm$ s)/M (P_{25}, P_{75})).

Indices	Time	Control group (n = 41)	Observation group (n = 39)	Z/t	p-value
LAD (mm)	Before treatment	33.82 ± 0.94	33.79 ± 1.02	0.112	0.911
	After 6 months of treatment	31.69 ± 0.88$^{\#\#}$	30.84 ± 0.58$^{\#\#}$	5.102	<0.001*
	Δ value	2.16 ± 1.31	2.95 ± 1.08	2.954	0.004*
LVPWT (mm)	Before treatment	11.06 ± 0.15	11.08 ± 0.15	0.633	0.529
	After 6 months of treatment	10.85 ± 0.19$^{\#}$	9.92 ± 0.18$^{\#\#}$	22.854	<0.001*
	Δ value	0.24 (0.10, 0.39)	1.20 (0.99, 1.33)	7.697	<0.001*
IVST (mm)	Before treatment	11.00 ± 0.21	11.06 ± 0.20	0.902	0.224
	After 6 months of treatment	10.48 ± 0.32	9.79 ± 0.18$^{\#\#}$	11.874	<0.001*
	Δ value	0.49 (0.20, 0.84)	1.27 (1.09, 1.52)	6.480	<0.001*
LVEDD (mm)	Before treatment	5.26 ± 0.05	5.25 ± 0.05	0.107	0.915
	After 6 months of treatment	5.15 ± 0.04$^{\#}$	4.94 ± 0.10$^{\#\#}$	12.439	<0.001*
	Δ value	0.11 ± 0.07	0.31 ± 0.11	10.115	<0.001*

Note: Δ value = |level after 6 months of treatment – level before treatment|.
*The difference was statistically significant.
Compared to the level before treatment level in the same group, $^{\#}p < 0.05$, $^{\#\#}p < 0.001$.
LAD, left atrial diameter; IVST, interventricular septal thickness; LVEDD, left ventricular end-diastolic diameter; LVPWT, left ventricular posterior wall thickness; M, median.

Comparison of Cardiac Function Indices Between the Two Groups

Before treatment initiation, there were no significant differences between the two groups in LVEF, FS, CO, SV, and E/A ($p > 0.05$). After 6 months of treatment, the observation group showed significant improvements in LVEF, FS, SV, CO, and E/A compared to the control group ($p < 0.05$, Table 3).

Table 3. Comparison of cardiac function indexes between the two groups (($\bar{x}\pm$ s)/M (P_{25}, P_{75})).

Indices	Time	Control group (n = 41)	Observation group (n = 39)	Z/*t*	*p*-value
LVEF (%)	Before treatment	52.37 ± 0.49	52.44 ± 0.50	0.633	0.529
	After 6 months of treatment	53.95 ± 0.89$^{\#\#}$	56.51 ± 0.94$^{\#\#}$	12.483	<0.001*
	Δ value	2.00 (1.00, 2.50)	4.00 (3.00, 5.00)	7.189	<0.001*
FS (%)	Before treatment	33.76 ± 2.11	33.26 ± 2.22	1.033	0.305
	After 6 months of treatment	35.02 ± 2.60$^{\#}$	39.00 ± 3.09$^{\#\#}$	6.229	<0.001*
	Δ value	2.00 (1.00, 2.50)	6.00 (3.00, 8.00)	4.654	<0.001*
SV (mL)	Before treatment	82.19 ± 5.18	80.41 ± 5.49	1.491	0.140
	After 6 months of treatment	82.35 ± 5.04	88.54 ± 6.72$^{\#\#}$	4.675	<0.001*
	Δ value	6.15 (3.61, 9.69)	9.24 (5.38, 13.84)	2.517	0.012*
CO (L/min)	Before treatment	7.05 ± 1.06	7.06 ± 1.00	0.059	0.953
	After 6 months of treatment	6.97 ± 1.01	7.74 ± 0.98$^{\#\#}$	3.466	0.001*
	Δ value	0.20 ± 0.12	0.68 ± 0.15	15.614	<0.001*
E/A	Before treatment	0.98 ± 0.08	0.97 ± 0.07	0.444	0.659
	After 6 months of treatment	1.02 ± 0.07$^{\#}$	1.09 ± 0.08$^{\#\#}$	3.925	<0.001*
	Δ value	0.08 (0.03, 0.11)	0.12 (0.05, 0.20)	2.324	0.020*

Note: Δ value = |level after 6 months of treatment – level before treatment|.
*The difference was statistically significant.
Compared to the level before treatment in the same group, $^{\#}p < 0.05$, $^{\#\#}p < 0.001$.
CO, cardiac output; FS, fractional shortening; LVEF, left ventricular ejection fraction; SV, stroke volume; E/A, peak mitral E-wave velocity/peak mitral A-wave velocity.

Table 4. Comparison of BNP and TnT levels between the two groups.

Indices	Time	Control group (n = 41)	Observation group (n = 39)	Z/*t*	*p*-value
BNP, ng/L	Before treatment	540.00 (407.5, 585.5)	481 (434, 562)	0.236	0.814
	After 6 months of treatment	439 (328.5, 494)$^{\#}$	382 (308, 423)$^{\#\#}$	2.128	0.033*
	Δ value	83 (45, 122)	116 (78, 176)	2.464	0.014*
TnT, ng/L	Before treatment	81 (61, 154)	83 (50, 114)	0.900	0.368
	After 6 months of treatment	68 (46.5, 134)	54 (35, 87)$^{\#}$	2.210	0.027*
	Δ value	11 (7.5, 18)	19 (9, 35)	2.611	0.009*

Note: Δ value = |level after 6 months of treatment – level before treatment|.
*The difference was statistically significant.
Compared to the level before treatment in the same group, $^{\#}p < 0.05$, $^{\#\#}p < 0.001$.
BNP, brain natriuretic peptide; TnT, troponin T.

Comparison of BNP and Troponin T Levels Between the Two Groups

Before treatment, there were no significant differences in BNP and troponin T (TnT) levels between the two groups ($p > 0.05$). After 6 months of treatment, the

Table 5. Comparison of serum biochemical indices between the two groups (($\bar{x}\pm$ s)/M (P_{25}, P_{75})).

Indices	Time	Control group (n = 41)	Observation group (n = 39)	Z/*t*	*p*-value
Scr (μmol/L)	Before treatment	1003.81 ± 160.57	963.84 ± 144.44	1.168	0.246
	After 6 months of treatment	416.48 ± 93.93$^{\#\#}$	330.69 ± 82.68$^{\#\#}$	4.328	<0.001*
	Δ value	572.69 ± 162.17	633.15 ± 63.26	–2.217	0.031*
BUN (mmol/L)	Before treatment	23.92 ± 1.62	23.71 ± 1.99	0.529	0.598
	After 6 months of treatment	18.99 ± 1.65$^{\#\#}$	12.69 ± 1.83$^{\#\#}$	16.174	<0.001*
	Δ value	4.93 ± 2.22	11.01 ± 3.17	–9.887	<0.001*
β2-MG (pg/mL)	Before treatment	25.55 ± 3.55	25.05 ± 3.94	0.598	0.552
	After 6 months of treatment	24.36 ± 3.26	14.08 ± 2.75$^{\#\#}$	15.221	<0.001*
	Δ value	4.34 ± 2.88	10.97± 4.42	–7.998	<0.001*
PTH (ng/L)	Before treatment	566.43 ± 70.06	565.84 ± 63.14	0.039	0.969
	After 6 months of treatment	460.88 ± 78.41$^{\#\#}$	334.03 ± 72.40$^{\#\#}$	7.507	<0.001*
	Δ value	101.53 (71.67, 193.60)	221.03 (175.12, 293.43)	–4.866	<0.001*

Note: Δ value = |level after 6 months of treatment – level before treatment|.

*The difference was statistically significant.

Compared to the level before treatment in the same group, $^{\#\#}p < 0.001$.

BUN, blood urea nitrogen; β2-MG, β2-microglobulin; PTH, parathyroid hormone; Scr, serum creatinine.

BNP level was significantly reduced in the observation group than in the control group ($p = 0.033$), with the observation group exhibiting a more pronounced change in BNP ($p = 0.014$). Furthermore, the TnT level was significantly lower in the observation group than in the control group ($p = 0.027$), with the observation group indicating greater change in TnT than in the control group ($p = 0.009$, Table 4).

Comparison of Serum Biochemical Indicators Between the Two Groups

Before treatment, there were no significant differences in Scr, BUN, β2-MG, and PTH levels between the two groups ($p > 0.05$). However, after 6 months of treatment, the observation group exhibited significant improvements in Scr, BUN, β2-MG, and PTH levels ($p < 0.05$, Table 5).

Comparison of Lipid Metabolism Indices Between the Two Groups

Before treatment, there were no significant differences in TC, TG, HDL, and LDL levels between the two groups ($p > 0.05$). However, after 6 months of treatment, the observation group demonstrated a substantial decrease in TC, TG, and LDL levels compared to the control group ($p < 0.001$). Furthermore, there was no statistically significant difference in HDL levels after 6 months of treatment between the two groups ($p = 0.915$), with the observation group exhibiting a higher Δ value ($p = 0.031$, Table 6).

Table 6. Comparison of lipid metabolism indices between the two groups ($(\bar{x} \pm s)$/M (P_{25}, P_{75})).

Indices	Time	Control group (n = 41)	Observation group (n = 39)	Z/t	p-value
TC (mmol/L)	Before treatment	5.06 ± 0.57	5.06 ± 0.53	0.038	0.969
	After 6 months of treatment	4.70 ± 0.93$^{\#}$	3.67 ± 0.97$^{\#\#}$	4.841	<0.001*
	Δ value	0.93 ± 0.62	1.54 ± 0.87	–3.575	0.001*
TG (mmol/L)	Before treatment	2.44 ± 0.34	2.38 ± 0.31	0.521	0.371
	After 6 months of treatment	2.04 ± 0.33$^{\#\#}$	1.61 ± 0.38$^{\#\#}$	5.337	<0.001*
	Δ value	0.32 (0.18, 0.61)	0.78 (0.38, 1.07)	–3.076	0.002*
HDL (mmol/L)	Before treatment	3.50 ± 0.56	3.24 ± 0.62	1.905	0.061
	After 6 months of treatment	4.49 ± 0.60$^{\#\#}$	4.47 ± 0.69$^{\#\#}$	0.107	0.915
	Δ value	0.92 (0.44, 1.53)	1.21 (1.13, 1.35)	2.157	0.031*
LDL (mmol/L)	Before treatment	3.50 ± 0.23	3.47 ± 0.19	0.520	0.604
	After 6 months of treatment	3.16 ± 0.25$^{\#\#}$	2.73 ± 0.25$^{\#\#}$	7.781	<0.001*
	Δ value	0.35 (0.17, 0.51)	0.71 (0.50, 0.99)	5.396	<0.001*

Note: Δ value = |level after 6 months of treatment – level before treatment|.
*The difference was statistically significant.
Compared to the level before treatment in the same group, $^{\#}p < 0.05$, $^{\#\#}p < 0.001$.
HDL, high-density lipoprotein; LDL, low-density lipoprotein; TC, total cholesterol; TG, triglycerides.

Table 7. Comparison of adverse event incidence between the two groups (n (%)).

Indices	Number of dialysis (time)	Hypertension (time)	Hypotension (time)	Arrhythmia (time)	Infection (time)
Control group (n = 41)	2952	312 (10.57%)	238 (8.06%)	23 (0.78%)	41 (1.39%)
Observation group (n = 39)	2808	224 (7.98%)	153 (5.45%)	11 (0.39%)	27 (0.96%)
χ^2	—	11.455	15.536	3.681	2.253
p-value	—	0.001	<0.001	0.055	0.133

Comparison of Adverse Event Incidence Between the Two Groups

A comparison of adverse event incidence during treatment between the control and observation groups demonstrated that hypertension was less frequent in the observation group (224 instances) than in the control group (312 instances) ($p = 0.001$). Similarly, the incidence of hypotension was significantly lower in the observation group (153 instances) than in the control group (238 instances) ($p < 0.001$). Furthermore, there were no significant differences in the incidence of arrhythmia ($p = 0.055$) and infection ($p = 0.133$) between the two groups (Table 7).

Discussion

HD is a primary therapeutic option for patients with severe acute renal failure and has been proven to improve survival rates (Cheetham et al, 2024). It works on the principle of a semi-permeable membrane to remove solutes and excess fluid from the plasma of uremic patients. However, HD primarily eliminates small water-soluble molecules, while most middle molecular weight uremic toxins remain in the plasma, increasing the likelihood of cardiovascular events and substantially reducing the quality of life (Zhang et al, 2022).

The present study retrospectively compared the combined effects of HD and HDF and found that compared with the control group, the observation group showed significant improvements in cardiac structure indices, cardiac function indicators (BNP and TnT), and serum biochemical parameters. Moreover, the incidence of adverse events was lower in the observation group than in the control group. These findings provide further insights into the effects of HD combined with HDF on various clinical indicators in uremic patients.

Effects of HD Combined With HDF on Cardiac Structure and Function in Uremic Patients

Uremia is a life-threatening condition, and HD alone is inadequate to effectively eliminate uremic toxins, leading to toxin accumulation and the progression of cardiovascular diseases (Falconi et al, 2021; Lim et al, 2021). Our study observed that HD combined with HDF significantly improved the cardiac structure and function in uremic patients, confirming the therapeutic benefits of this combined treatment. A previous study by Xu et al (2023) reported that combining hemodialysis with hemofiltration is an effective method for treating uremia, as it significantly improves cardiac function, promotes toxin clearance, and has fewer adverse reactions, making it a safe approach for clinical application. Our study further demonstrated

that HD combined with HDF is more effective than HD alone in improving echocardiographic parameters, such as LAD, LVPWT, IVST, and LVEDD. Additionally, our study evaluated key biomarkers of myocardial stress and injury, particularly BNP and high-sensitivity cardiac troponin T (hsTnT), which are crucial indices of subclinical cardiac involvement in uremic patients. Accumulation of uremic toxins has been found to induce myocardial injury and fibrosis (Frąk et al, 2024), resulting in the progression of heart failure and myocardial injury. BNP, a well-recognized marker of cardiac wall stress, and hsTnT, an indicator of myocardial injury, were comparatively assessed between the two groups, indicating no significant differences in the baseline levels of cardiac stress and injury. However, after 6 months of treatment, BNP levels in the observation group were significantly reduced than those in the control group, with a similar decrease in hsTnT levels. These results further support the improved ability of combining HD with HDF to relieve myocardial stress and injury, aligning with the findings of Ethier et al (2019). Their study revealed that, compared to the hemodialysis group, the median change in hsTnT values was –3 ng/L in the HDF group, while in the HD group, it was +8 ng/L. Furthermore, a meta-analysis by Guimarães et al (2024) reported that patients receiving HDF had a reduced cardiovascular mortality rate than those undergoing HD alone. Notably, HD combined with HDF treatment also demonstrated a better safety profile than HD alone, further reinforcing HDF's clinical utility.

Effect of HD Combined With HDF on Metabolic Wastes in Uremic Patients

The results of this study indicate that HD combined with HDF treatment is highly effective in eliminating toxins in uremia patients, significantly reducing Scr, BUN, β2-MG, and PTH levels while improving renal function. Scr and BUN are crucial renal function indicators, with Scr being the ultimate metabolite of protein breakdown and BUN a product of creatine hydrolysates (Lerink et al, 2022). The kidney is the primary excretory organ for both BUN and Scr. A decline in renal function results in a substantial increase in their levels, suggesting severe renal function impairment (Al Jameil, 2019). HDF, a blood purification method for eliminating macromolecules, uses a high-permeability dialysis membrane to filter out multiple toxins while improving the ultrafiltration rate when combined with hemodialysis. This combined approach not only effectively removes small molecular toxins through diffusion but also clears middle and high molecular weight toxins, thereby reducing metabolic waste accumulation in patients. Supporting our findings, a study by Nenova et al (2024) reported that HDF offers higher dialysis adequacy than HD.

Effect of HD-HDF Combined Approach on Lipid Metabolism in Uremic Patients

Patients with renal insufficiency usually experience lipid metabolism disorders in the early stage of kidney disease (Gai et al, 2019). Furthermore, impaired renal function is linked to a high incidence of dyslipidemia, which promotes atherosclerosis and increases the risk of cardiovascular disease. The results of this study revealed that patients undergoing HD combined with HDF demonstrated a signifi-

cant reduction in total TC, TG, HDL, and LDL levels compared to those receiving HD alone. These findings suggest that the combined approach effectively improves lipid metabolism and reduces cardiovascular disease risk in uremic patients. Lipid metabolism disorder is a common complication in uremic patients (Tauqeer et al, 2017), primarily manifested by elevated TC and TG levels. It is closely linked to the accumulation of uremic toxins, which affect lipid metabolism enzyme activity and contribute to metabolic imbalance (Su et al, 2018). Furthermore, this combined approach further improves the ultrafiltration rate, facilitating enhanced lipid metabolism and toxin clearance.

Research Limitations

First, due to research condition constraints and methods, this study included only 80 patients from the same hospital. The small sample size may affect the generalizability of these results and increase the risk of Type II errors. Although the calculated sample size was sufficient to achieve statistical significance for the primary outcome, a larger sample size could improve statistical power and result robustness. Furthermore, the 6-month follow-up period provided valuable insights into the short-term effects of HD and HDF combined approach on cardiac structure, function, and metabolic indicators. However, this duration may not fully capture the long-term benefits or potential late-onset impacts of the treatment, particularly in patients with chronic conditions like uremia. Therefore, a longer follow-up is needed to evaluate the sustained effect of HD and HDF combined approach on cardiac remodeling and disease progression. The retrospective nature of the study design also limited its ability to predefine follow-up durations. Future prospective studies with larger sample sizes and extended follow-up periods will be crucial to validate these findings and provide more comprehensive insights into the long-term outcomes of this combined treatment strategy. Additionally, the effects of this combined approach on other important organs and systems in uremic patients, such as the lungs and bones, need further investigation. Exploring these aspects could offer valuable clinical information and contribute to more comprehensive management approaches for uremic patients.

Conclusion

This retrospective study analyzed the effects of HD combined with HDF on cardiac structure and function and serum biochemical indices in uremic patients and found that this combined approach improves cardiac structure and function, reduces metabolic wastes, and improves lipid metabolism. However, the relatively short follow-up period limits the evaluation of long-term outcomes. Future research with extended follow-up periods is essential to assess the long-term efficacy, reliability, and overall impact of this combined treatment strategy.

Key Points

- Hemodialysis combined with hemodiafiltration improves the cardiac structure and function in uremic patients.
- Hemodialysis combined with hemodiafiltration reduces metabolic wastes like serum creatinine, β2-microglobulin, and blood urea nitrogen in uremic patients.
- Hemodialysis combined with hemodiafiltration reduces the blood lipid levels in uremic patients.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

HYF designed the study; all authors conducted the study; YHX, HYL and LJZ collected and analyzed the data. HYF and JDW participated in drafting the manuscript, and all authors contributed to the critical revision of the manuscript for important intellectual content. All authors gave final approval of the version to be published. All authors participated fully in the work, took public responsibility for appropriate portions of the content, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

The study design adhered to the principles of the Declaration of Helsinki, and informed consent was obtained from each participant. This study was approved by the Medical Ethics Committee of the Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University (Approval No.: K20240741).

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Conflict of Interest

The authors declare no conflict of interest.

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