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Research on the combined impact of high-flux dialysis and levocarnitine on the functionality of arteriovenous fistulas in patients undergoing maintenance hemodialysis

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Abstract: To explore the influence of levocarnitine on arteriovenous fistula (AVF) function in patients undergoing high-flux dialysis and delve into its potential mechanisms. Complication Reduction: The treatment group had markedly lower incidences of vascular stenosis (4.69% vs. 20%), thrombosis (3.13% vs. 15%), poor venous return (6.25% vs. 18.33%), and pre-dialysis hypotension (7.81% vs. 23.33%) (all $P < 0.05$). Hematological Benefits: Significant improvements in hemoglobin (11.57 ± 1.63 vs. 10.38 ± 1.49g/dL) and red blood cell count (3.89 ± 0.51 vs. 3.53 ± 0.46 $\times 10^{12}$/L) were observed in the treatment group ($P < 0.001$), alongside reduced white blood cell counts (6.05 ± 1.49 vs. 6.23 ± 1.60 $\times 10^{9}$/L, $P = 0.006$). Quality of Life: Karnofsky Performance Scale (KPS) scores were significantly higher in the treatment group at both 1-month ($P < 0.01$) and 3-month follow-ups ($P < 0.01$). In the context of high-flux hemodialysis, supplementing with levocarnitine can appreciably improve AVF function in ESRD patients, mitigate the occurrence of complications, and potentially enhance the quality of life by alleviating dialysis-related issues. Levocarnitine emerges as a promising adjunctive therapy for patients with compromised AVF function.

Keywords: Arteriovenous fistula, high-flux dialysis, levocarnitine, maintenance hemodialysis, vascular complications

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INTRODUCTION

Maintenance hemodialysis (MHD) is a crucial treatment method for extending the life of patients with end-stage renal disease (ESRD) (Abe M, 2021). As a preferred vascular access method, the functional stability of an arteriovenous fistula (AVF) significantly impacts dialysis efficiency and patient survival quality (Battaglia Y, 2025). Low-flux dialysis often limits treatment effectiveness due to its limited clearance of medium and large molecular substances (Bignardi PR, 2024). With the application of high-flux dialysis membranes, dialysis efficacy has improved, providing better clearance of medium molecular substances for patients, but it also presents a series of new problems and challenges (Caskey FJ, 2022).

During high-flux dialysis treatment, the increased efficiency in clearing small molecular substances may lead to a reduction in the levels of levocarnitine in patients. Levocarnitine is essential for the intracellular transport of long-chain fatty acids into the mitochondria, and its deficiency in dialysis patients has been associated with numerous complications, including muscle weakness, cardiac dysfunction and metabolic disorders and Alternative Medicine EC. (2023). Retracted: Effects of High Flux Hemodialysis Combined with L-Carnitine on Microinflammation and Arteriovenous Fistula in Maintenance Hemodialysis Patients. Evidence-based complementary and alternative medicine: eCAM, 2023, 9846504). Additionally, vascular access function impairment is a common and serious issue in hemodialysis patients, leading to AVF dysfunction and related complications (Morgans HA, 2021).

Current research suggests that levocarnitine may have a protective effect on AVF function through various mechanisms, including improving mitochondrial function, promoting normalization of blood lipid levels, reducing oxidative stress and exhibiting anti-inflammatory effects, thereby affecting vascular endothelial function and anticoagulation status (Chen CY, 2022) However, other strategies have also been investigated to improve AVF functionality in hemodialysis patients. For example, the use of local drug delivery systems (such as heparin or prostacyclin) to enhance blood flow and reduce thrombus formation has shown promise in preventing AVF stenosis and maintaining long-term patency (Chi XG, 2021). Additionally, recent studies have explored the role of mechanical stimulation through exercise and vascular remodeling techniques to improve the structural integrity and function of AVFs (De Schuyter K, 2021). Another approach includes optimizing the management of risk factors such as diabetes and hypertension, which can significantly influence AVF maturation and longevity (Huang W, 2024).

Despite the availability of these strategies, challenges remain, such as limited efficacy of low-flux dialysis, risks of medication side effects, and incomplete understanding of long-term outcomes (Kandi M, 2022). High-flux dialysis combined with Levocarnitine supplementation has been proposed as a potentially more effective intervention,

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as it may improve the clearance of toxins while addressing Levocarnitine deficiency, which is a common issue in dialysis patients (Kandi M, 2022). This combination therapy may offer complementary benefits in terms of mitochondrial function, oxidative stress reduction, and vascular protection, which are critical factors for maintaining AVF functionality.

In the field of hemodialysis, improving AVF function through pharmacological intervention has been a focal point and challenge of research (Kim HJ, 2021). This study aims to evaluate the combined effect of high-flux dialysis treatment and levocarnitine supplementation on AVF function, exploring the impact of this combined strategy on the stability of AVF function, the incidence of AVF vascular complications, and the quality of life in ESRD patients. Through a retrospective study design, clinical data from ESRD patients who received high-flux dialysis combined with levocarnitine treatment at Third Affiliated Hospital of Qiqihar Medical College over the past two years were collected, and differences in AVF function, complication incidence, and hematological indicators were comparatively analyzed. This study provides new insights and evidence to support the optimization of hemodialysis treatment regimens for ESRD patients through an in-depth investigation of the combined application of high-flux dialysis and levocarnitine supplementation.

MATERIALS AND METHODS

This retrospective study included 124 patients with end-stage renal disease (ESRD) undergoing maintenance hemodialysis at Third Affiliated Hospital of Qiqihar Medical Collegel from January 2023 to December 2024. All patients followed standardized procedures for arteriovenous fistula creation and dialysis operation. Patients were divided into two groups based on the treatment method: the treatment group, consisting of 64 patients, received levocarnitine in addition to high-flux hemodialysis; the control group, consisting of 60 patients, received only high-flux hemodialysis. This study was approved by the ethics committee of Third Affiliated Hospital of Qiqihar Medical College, No. 2024LL-20.

Inclusion criteria were as follows: patients diagnosed with end-stage renal disease (ICD-10 code: N18.0) who had undergone regular intermittent high-flow hemodialysis (HFHD) at Third Affiliated Hospital of Qiqihar Medical College for more than three months; aged between 18 and 80 years; with well-matured and functional arteriovenous fistulas suitable for dialysis needle placement; patients or their legal guardians signed informed consent; agreed to follow up throughout the study period.

Exclusion criteria were as follows: patients with severe complications such as other major organ dysfunction, malignant tumors, or active infectious diseases; patients who had undergone kidney transplantation in the past six months; patients with a history of using levocarnitine or other similar drugs; patients with psychological disorders or cognitive impairments who could not understand the study protocol or cooperate with the study; patients who could not obtain suitable arteriovenous fistulas and required long-term catheter dialysis.

In this study, all enrolled patients adhered to standard blood pressure management protocols, including necessary antihypertensive drug treatments. During dialysis, patients were supplemented with iron, folic acid, and vitamin B12 as needed, and erythropoietin (EPO) interventions were administered. Recombinant human erythropoietin injection-Epitin, Sinovac Biotech Co., Ltd. (approval number: S20000008), was initially administered at a dose of 3000 units three times a week. When patients' hemoglobin levels reached above 120g/L (females) or 130g/L (males), or when hematocrit increased to the range of 33% to 36%, the dose of erythropoiesis-stimulating agents was appropriately reduced to maintain hemoglobin levels between 110 and 120g/L and hematocrit between 30% and 35%.

In the control group, patients received only high-flux hemodialysis using polysulfone membrane hollow fiber dialyzers HF15 provided by Weigao Group Shandong Co., Ltd., with dialysis frequency set at three times a week. The dialyzer had an effective membrane area of 1.5 square meters and an ultrafiltration coefficient of 50 mL/(mmHg·hour). The dialysate used a bicarbonate formula, and low-molecular-weight heparin was used during anticoagulation. The dialysate flow rate was adjusted to 500-800mL/min and the blood flow rate was maintained at 200-250mL/min, with each dialysis session lasting 4 hours.

In the treatment group, in addition to the high-flux hemodialysis received by the control group, patients were immediately given an intravenous injection of levocarnitine after dialysis, provided by Shandong Yuman Kun Biotechnology Co., Ltd. (approval number: H20233153), at a specification of 5mL:1g. The treatment dosage was 1 g per session, three times a week, for a duration of three months. Through this method of grouped treatment, this study aimed to compare and analyze the efficacy differences in improving arteriovenous fistula function between high-flux dialysis and levocarnitine.

Arteriovenous fistula blood flow is a key indicator of blood clearance efficiency. AVF blood flow was measured using Doppler ultrasound equipment (model: Philips EPIQ7C) before (T0) and after (T1) dialysis. The diameter of AVF vessels was assessed using ultrasound imaging equipment (model: Konica HS1) before (T0) and after (T1) dialysis to evaluate changes in vessel diameter. Hematological indicators of patients, including hemoglobin level, red blood cell count, and white blood cell count, were tested using an automatic blood analyzer (models: Mindray 7500CS, Beckman AU5821, Beckman Image800) before treatment (T0) and at the first month (M1) after treatment.

Table 1: Baseline Characteristics of Patients

	n	Age (years)	Gender (M/F)	Disease Duration (years)	Kt/V
Treatment Group	64	58.45±12.36	35/29	5.67±3.12	1.53±0.24
Control Group	60	59.22±11.89	33/27	5.39±3.26	1.49±0.28
t / $\chi2$		0.457	0.210	0.582	1.008
P		0.648	0.647	0.561	0.315

Mean ± SD

Table 2: Comparison of AVF Function Indicators Before and After Treatment

	n	AVF Blood Flow (mL/min)		AVF Vessel Diameter (mm)	
		T0	T1	T0	T1
Treatment Group	64	122.75±18.62	148.98±20.45[a]	4.22±0.79	4.93±0.85[a]
Control Group	60	120.58±17.33	131.41±18.67[a]	4.25±0.81	4.30±0.83[a]
t		0.467	8.764	-0.145	5.372
P		0.642	<0.001	0.885	<0.001

Note: Compared to before treatment, a $P < 0.05$. Mean ± SD

Table 3: Incidence of Complications [n(%)]

	n	Vascular Stenosis	Thrombosis	Poor Venous Return	Arterial Blood Pressure Below Specified Value Before Dialysis
Treatment Group	64	3 (4.69%)	2 (3.13%)	4 (6.25%)	5 (7.81%)
Control Group	60	12 (20%)	9 (15%)	11 (18.33%)	14 (23.33%)
$\chi2$		6.292	5.017	4.086	5.662
P		0.012	0.025	0.043	0.017

Table 4: Changes in Hematological Indicators

	n	Hemoglobin (g/dL)		Red Blood Cell Count ($\times10^{12}$/L)		White Blood Cell Count ($\times10^{9}$/L)	
		T0	M1	T0	M1	T0	M1
Treatment Group	64	7.21±1.38	11.57±1.63[a]	2.68±0.45	3.89±0.51[a]	6.70±1.58	6.05±1.49[a]
Control Group	60	7.22±1.45	10.38±1.49[a]	2.63±0.47	3.53±0.46[a]	6.75±1.61	6.23±1.60[a]
t		0.512	5.144	0.430	4.899	0.637	2.803
P		0.609	<0.001	0.667	<0.001	0.525	0.006

Note: Compared to before treatment, a$P < 0.05$. Mean ± SD

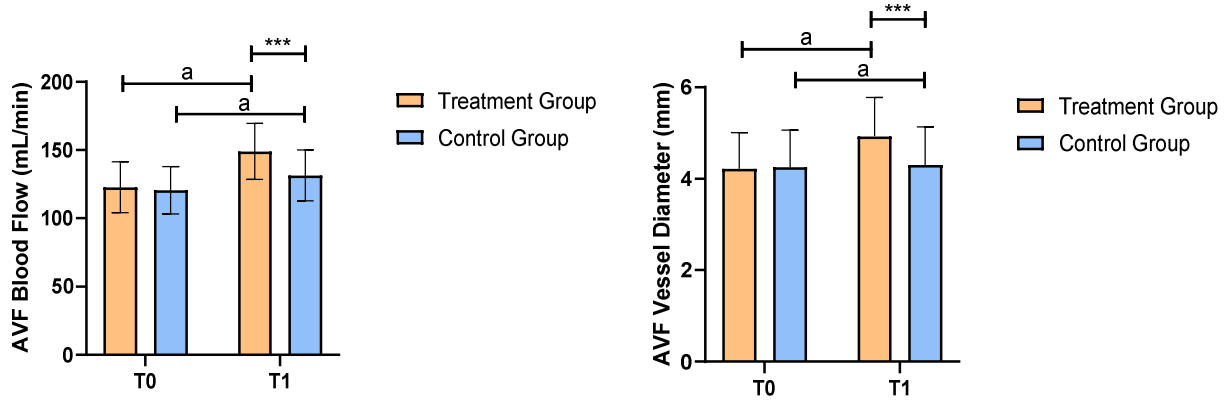

Fig. 1: Comparison of AVF Function Indicators Before and After Treatment. Compared to before treatment, a$P < 0.05$. ***$P < 0.05$ between the two groups. Mean ± SD

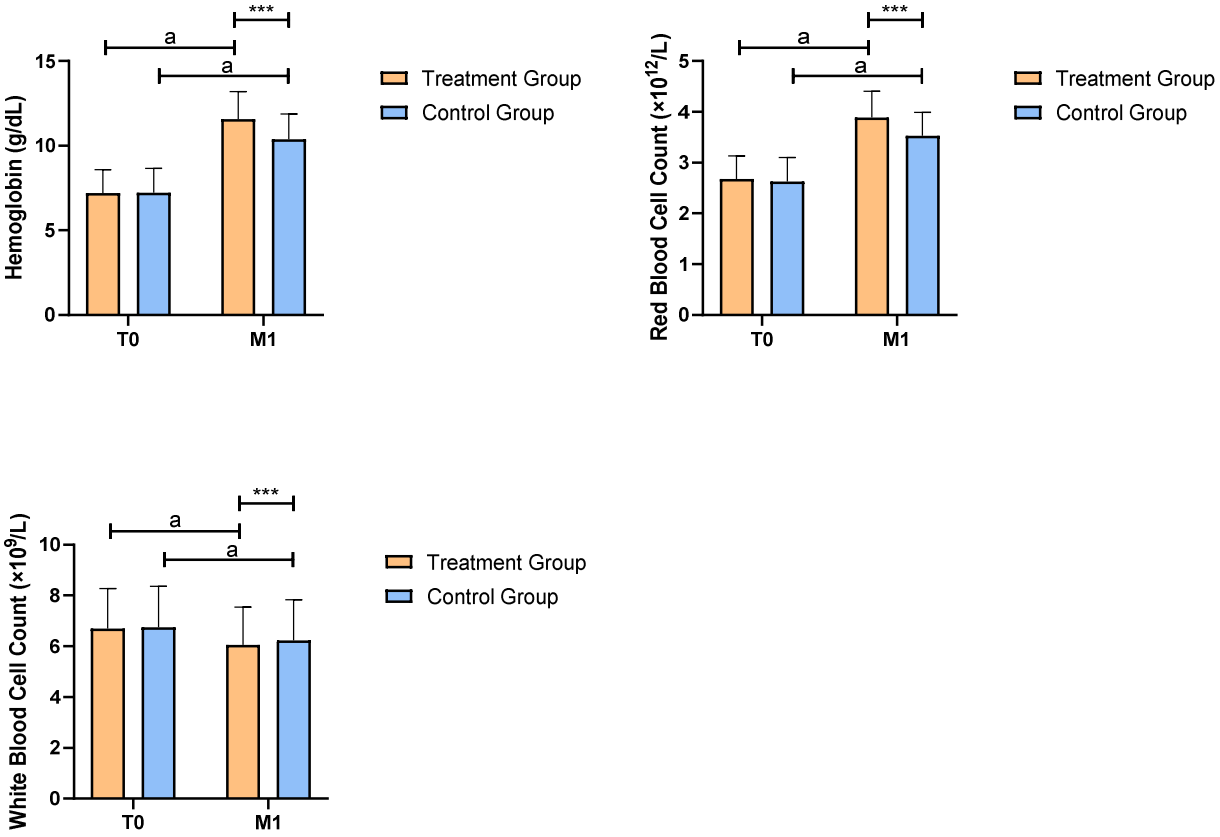

Fig. 2: Changes in Hematological Indicators. Compared to before treatment, a$P < 0.05$. ***$P < 0.05$ between the two groups. Mean ± SD

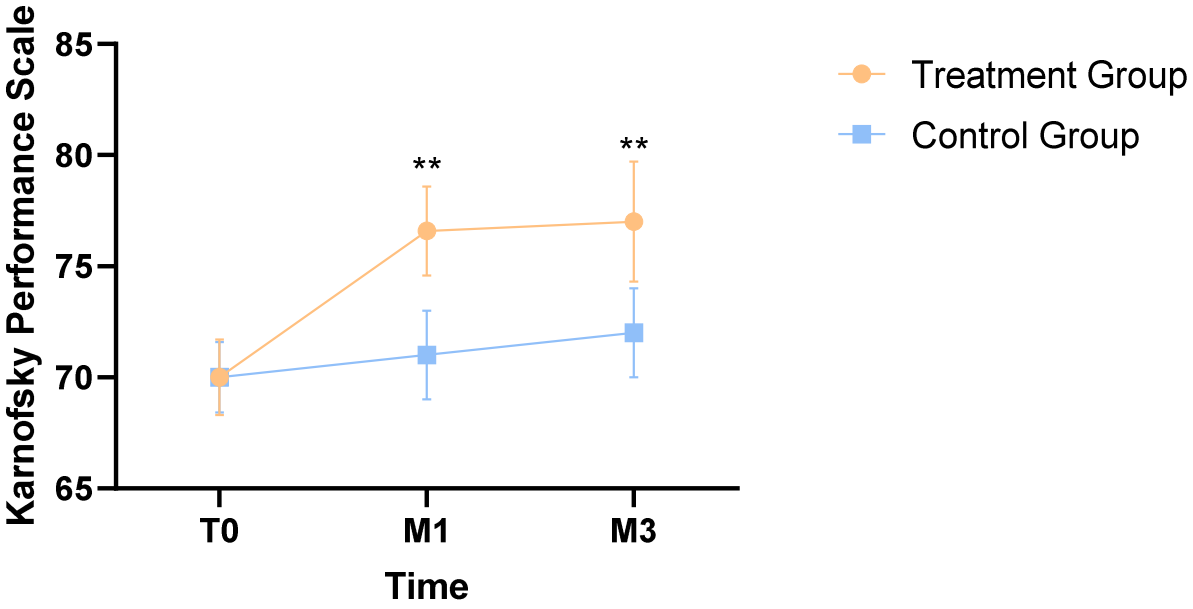

Fig. 3: Karnofsky Performance Scale. The treatment group had significantly higher scores at M1 and M3 compared to the control group (**$P < 0.01$)

Incidence of AVF vascular complications, such as vascular stenosis, thrombosis, and poor venous return, was monitored and recorded by the nursing team during each dialysis session. The Karnofsky Performance Scale (KPS) was used to assess patients' functional status and quality of life, with scores ranging from 0 to 100, where higher scores indicated better status. This assessment was performed at the initial evaluation (T1) and at the first (M1) and third (M3) months after treatment.

STATISTICAL ANALYSIS

Continuous variables were presented as mean ± standard deviation (SD) and analyzed using t-tests for differences; non-continuous variables were presented as frequencies and percentages and analyzed using chi-square tests or Fisher's exact tests. All hypothesis tests were set at a 5% significance level, with $P < 0.05$ considered statistically significant. For multiple comparisons, Bonferroni correction was applied to adjust P-values to avoid an increase in Type I errors. Data analysis was performed using the SPSS statistical software package (IBM SPSS Statistics, version 26.0, IBM Corp., Armonk, NY, USA).

RESULTS

Table 1 shows the baseline characteristics of the treatment and control groups, including age, gender, disease duration, and dialysis efficiency indicator Kt/V. The results indicate that there were no statistically significant differences between the two groups in terms of age, gender distribution, disease duration, and Kt/V, suggesting that the patient data were comparable.

Table 2 presents the AVF function indicators before (T0) and after (T1) treatment, including AVF blood flow and AVF vessel diameter. The results show that the treatment group had significantly higher improvements in AVF blood flow and vessel diameter compared to the control group after treatment ($P < 0.001$). This suggests that the addition of levocarnitine had a significant effect on improving AVF function.

Table 3 describes the incidence of AVF vascular complications in both groups, including vascular stenosis, thrombosis, poor venous return, and arterial blood pressure below the specified value before dialysis. The results show that the treatment group had a lower incidence of these complications compared to the control group ($P < 0.05$).

Table 4 shows the changes in hematological indicators before treatment (T0) and at the first month (M1) after treatment, including hemoglobin levels, red blood cell count, and white blood cell count. Compared to the control group, the treatment group had significant improvements in hemoglobin levels and red blood cell count, while white blood cell count significantly decreased ($P < 0.01$).

The KPS scoring system was used to evaluate the overall condition of patients in both groups before treatment (T0), at the first month (M1), and at the third month (M3) after treatment, as shown in fig. 1-3. The treatment group had significantly higher scores at M1 and M3 compared to the control group ($P < 0.01$).

DISCUSSION

Arteriovenous fistula (AVF) is the preferred long-term vascular access for hemodialysis patients, and its functional stability is crucial. Compared to other types of vascular access, AVF has a longer dialysis lifespan and lower complication rates. However, stenosis and thrombosis remain significant challenges in this field (Lim JH, 2020).

Studies have shown that the patency rate of autologous AVF is about 65% within 2 years, and it decreases to 48% by the fourth year (Rodriguez, A., 2021). Current research indicates that possible factors leading to AVF stenosis include diabetes, hypertension, lipid metabolism disorders, and uremic toxins, with intimal hyperplasia being a critical factor. Further studies have found that intimal hyperplasia is closely related to a micro-inflammatory state. This state, triggered by non-pathogenic microbial infections, manifests as elevated levels of circulating inflammatory proteins and cytokines, representing a hidden, persistent aseptic inflammation that can lead to various complications, with high-sensitivity C-reactive protein (hs-CRP) being a marker of micro-inflammation (Wang Y, 2023; Wardoyo EY, 2022). In hemodialysis patients, about 35% to 65% exhibit a micro-inflammatory state, which promotes platelet activation, leukocyte adhesion, migration and proliferation of smooth muscle cells and myofibroblasts from the media to the intima, and extracellular matrix deposition (Yang J, 2022). These pathological processes further induce intimal hyperplasia, AVF stenosis, and even functional failure. Therefore, monitoring and managing inflammation markers are key to reducing complications and improving AVF outcomes in hemodialysis patients (Zakrzewska A, 2024).

The accumulation of metabolic endotoxins in maintenance hemodialysis patients, including small, medium, and large molecular toxins, particularly medium and large molecular toxins that cannot be removed by conventional dialysis, is a key cause of complications. High-flux hemodialysis can remove solutes through diffusion, convection, and adsorption, with its superior adsorption performance and larger pore size being particularly effective in removing medium and large molecular toxins (Zelenitsky SA and Ariano RE. (2022). L-carnitine is an important cofactor in energy metabolism in mammals, ensuring the normal operation of the tricarboxylic acid cycle, but it can be removed as a small molecule during dialysis, affecting the patient's energy metabolism. Studies have shown that L-carnitine not only has anti-inflammatory properties and

promotes erythrocyte antioxidant responses, but also enhances fatty acid metabolism and improves the micro-inflammatory state (Rehman S, 2025; Rehman S, 2024). This study found significant improvements in red blood cell count and hemoglobin levels in patients after treatment. High-flux hemodialysis can remove substances that inhibit bone marrow erythroid differentiation and enhance the efficacy of EPO, thereby alleviating erythropoiesis disorders. It can also remove inflammatory factors, improving the internal environment. L-carnitine works through antioxidation, protecting red blood cells, promoting protein synthesis, and improving cellular metabolism.

This study investigated the combined effects of high-flux dialysis with L-carnitine treatment on AVF function in maintenance hemodialysis. The results showed that the treatment group, which received additional L-carnitine treatment alongside high-flux dialysis, had significantly improved AVF blood flow and vessel diameter, and a lower incidence of AVF vascular complications compared to the control group. Additionally, the treatment group showed lower white blood cell counts and higher KPS scores, suggesting that L-carnitine not only improved dialysis effectiveness but also potentially enhanced the patients' quality of life.

In the study, the AVF blood flow and vessel diameter of the treatment group were significantly higher than those of the control group, consistent with previous research findings (Zhao X, 2024). This previous study also reported that high-flux hemodialysis combined with L-carnitine treatment significantly improved cardiac function, enhanced quality of life, reduced AVF complications and improved the prognosis of patients receiving maintenance hemodialysis. This combined treatment significantly lowered the levels of micro-inflammatory markers such as hs-CRP and TNF-α, indicating an alleviation of the micro-inflammatory state.

Levocarnitine (L-carnitine) exerts antioxidative and anti-inflammatory effects through multiple molecular pathways. Nitric Oxide (NO) Modulation: L-carnitine enhances endothelial nitric oxide synthase (eNOS) activity, increasing NO production, which improves vasodilation and reduces endothelial dysfunction. NO also inhibits leukocyte adhesion and smooth muscle cell proliferation, key processes in intimal hyperplasia (Takashima H, 2021). NF-κB Pathway Suppression: L-carnitine downregulates the nuclear factor-kappa B (NF-κB) pathway, reducing the expression of pro-inflammatory cytokines such as TNF-α, IL-6, and IL-1β, thereby attenuating systemic inflammation (Zheng Y, 2020). Reactive Oxygen Species (ROS) Scavenging: By neutralizing ROS and enhancing mitochondrial fatty acid oxidation, L-carnitine reduces oxidative stress. This preserves cellular integrity and inhibits ROS-induced activation of pro-inflammatory pathways (Zhou J and Yang T (2020). Nrf2 Pathway Activation: L-carnitine activates the nuclear factor erythroid 2-related factor 2 (Nrf2) pathway, upregulating antioxidant enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GPx), which counteract oxidative damage (Morgans, H. A., 2021). These mechanisms collectively mitigate micro-inflammatory states and oxidative stress, critical contributors to AVF dysfunction. In this study, the incidence of AVF vascular complications in the treatment group was significantly lower than that in the control group, further supporting the vascular protective role of L-carnitine.

This study provides a strong supplement to the systematic evaluation of L-carnitine use in dialysis patients, but it also has some limitations. Retrospective Design: Potential selection and information biases may affect result reliability. Single-Center Sample: Although the sample size was adequate, the lack of multicenter recruitment limits generalizability. Short Follow-Up Duration: Long-term effects of combined therapy on AVF patency beyond the study period remain unclear. Biomarker Gaps: Inflammatory markers like IL-6 or NF-κB were not measured, restricting mechanistic insights. Future studies should address these through prospective, randomized controlled trials with extended follow-ups and biomarker profiling.

CONCLUSION

This study demonstrates that high-flux dialysis combined with L-carnitine significantly improves AVF functionality, reduces complications, and enhances quality of life in hemodialysis patients. The antioxidative and anti-inflammatory properties of L-carnitine, mediated via NO, NF-κB, and Nrf2 pathways, likely contribute to these benefits. However, prospective multicenter trials are needed to validate these findings and explore long-term efficacy. Future research should also investigate optimal dosing regimens, molecular interactions, and cost-effectiveness to establish L-carnitine as a standardized adjunct therapy. Integrating mechanistic studies with clinical outcomes will further elucidate its role in vascular protection and dialysis care.

Conflict of Interest Statement

The authors declare that they have no competing interests

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