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The impact of low-protein diet on residual renal function in dialysis patients: a systematic review and metaanalysis

Jingyi Xie[1†], Xiaoqin Liu[1†], Yue Ling[1], Shuwang Ge[1*†] and Ying Yao[1*†]

Abstract

Objective A low-protein diet is essential for the nutritional management of chronic kidney diseases as it can reduce renal burden. However, the effect of low-protein diets on dialysis patients compared to pre-dialysis patients remains unclear. This study aims to compare residual renal function among dialysis patients following a low-protein diet versus a normal diet, offering valuable insights into the optimal nutritional strategy for preserving residual renal function.

Methods This meta-analysis has been registered on PROSPERO, an international registry of prospective systematic reviews. We conducted a comprehensive and systematic literature search using PubMed, Cochrane Library and Web of Science (WOS). Our search strategy was designed to discover all relevant studies investigating the influence of low-protein diets on residual renal function among dialysis patients. Four studies met the inclusion criteria. Heterogeneity was discussed through subgroup analysis of dialysis method, the addition of ketoacid and other relevant factors.

Results We included four prospective studies of low-protein diets among dialysis patients, each of which included at least 40 participants. Individuals receiving a 12-months low-protein diet had a higher GFR (MD = 1.37 ml/min; 95% CI:0.18 to 2.55), while daily urine volume decreasing more slowly (MD = 660 ml; 95% CI: 110 to 1210). In addition, dialysis patients undergoing a low-protein diet for 4 or 12 months had reduced serum phosphorus (MD=-0.74 g/dl; 95% CI: -1.04 to -0.45). Their serum albumin was higher than dialysis patients received a free-choice diet (MD = 4.00 g/dl; 95% CI: 2.46 to 5.54).

Conclusion Dialysis patients who adhere to a long-term low-protein diet may have a positive effect on residual kidney function. In addition, dialysis patients receiving a low-protein diet increased serum albumin, reduced serum phosphorus levels, and maintained a better nutritional status and electrolyte balance.

Keywords Low-protein diet, Renal function, Hemodialysis, Peritoneal dialysis, Nutrition

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Introduction

As a significant global public health issue, chronic kidney disease (CKD) affects millions of people worldwide [1, 2]. The progression of CKD can result in a gradual deterioration of renal function and ultimately come to end-stage renal disease (ESKD), requiring life-sustaining peritoneal dialysis or hemodialysis [3]. While these methods effectively remove waste and excess water from the body, they also present various complications and reduce quality of life [4].

Residual renal function, the portion that remains functional during dialysis, plays a crucial role in fluid and electrolyte balance control, reducing dialysis-related complications, improving quality of life, and increasing survival rates [5, 6]. Therefore, preserving residual renal function has become a key objective in treating CKD patients.

In the nutritional management of kidney disease, low-protein diets have always been an important consideration [7]. These diets are designed to alleviate strain on the kidneys and slow down further decline in renal function. For dialysis patients specifically [8], appropriate protein intake is essential for maintaining nutritional status, enhancing treatment outcomes, and safeguarding residual renal function. However, in published meta-analyses, it is controversial whether a low-protein diet has an impact on residual renal function among CKD patients [9, 10]. At the same time, studies among dialysis patients on the influence of low-protein diets on residual renal function have produced inconsistent results [11–13] due to factors such as study design, patient characteristics, and dialysis mode. The safety of low-protein diets also needs to be further explored due to possible malnutrition and other problems [14–16].

As such, this meta-analysis aims to comprehensively assess the influence of low-protein diets on dialysis patients' residual renal function and potential safety issues. By rigorously screening existing literature for data extraction and quality assessment purposes, this study will further delve into the mechanism by which low-protein diets affect residual renal function in this specific population as well as their potential clinical value so as to provide a more robust evidence base for nutritional treatment strategies targeting the progression of kidney diseases.

Materials and methods

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 Statement and Meta-Analysis of Observational Studies in Epidemiology (MOOSE) group [17, 18]. We registered the protocol on PROSPERO (CRD42024507043).

Search strategy

A search was performed by two reviewers (XJY and LXQ) using three databases from the establishment (PubMed 1879, Cochrane Library 1993, Web of Science 1997) until January 9, 2024. The search terms included dialysis [Mesh], peritoneal dialysis [Mesh], hemodialysis [Mesh], renal function, renal function, protein-restricted, dietary proteins, low-protein diet and protein restriction. EndNote X9 was utilized to manage these retrieved studies.

Selection criteria

We defined dietary protein intake (DPI) of 0.6–0.8 g/kg/day as low protein diet. The inclusion criteria for the studies were as follows: (i) participants were aged ≥ 18 years; (ii) randomized controlled trial (RCT) and prospective study; (iii) patients undergoing peritoneal dialysis (PD) or hemodialysis (HD); (iv) English articles.

Studies were excluded based on these exclusion criteria: (i) patients with evidence of infection or inflammation; vomiting, persistent anorexia or diarrhea; concurrent wasting disease like tuberculosis. (ii) participants received dialysis because of acute kidney injury (AKI) or AKI; (iii) publications were reviews, case reports, commentary, conference articles and animal studies; (iv) publications without abstracts or full texts.

Data extraction and quality assessment

By two reviewers (XJY and LXQ), the characteristics were extracted independently. The primary outcome was residual renal function which measured by daily urine volume and glomerular filtration rate (GFR). GFR is defined as the average of creatinine and urea clearances measured over a 24-hour urine collection. And the secondary outcomes were KT/V, the number of adverse events (infection, cardiovascular event or hospitalization for other reasons), patients dropped for declining of residual renal function, all-cause mortality, and nutritive index (serum phosphorus, serum calcium serum albumin).

We extracted data from included studies: author name, publication year, region, study design, inclusion criteria, sample size, gender, average age, follow-up time, treatment, and data pertaining to outcome variables.

For randomized controlled trials, we used the Cochrane Collaboration tool [19] to evaluate the quality. It includes allocation concealment, random sequence generation, blinding of outcome assessment, and other biases, assigning low risk, high risk, or unclear risk. And we used the Newcastle-Ottawa (NCO) scale for non-RCTs and prospective observational study [20, 21]. It includes selection, comparability and outcome.

Statistical analyses

We used Review Manager (RevMan) for the meta-analysis. Calculate the standard deviation (SD) and 95%

confidence intervals (95% CIs) for continuous variables. Among the included studies' results, heterogeneity was quantified with the Q statistic and quantified by the I^2index. Based on the outcomes of these statistical tests, we adopted different models for data synthesis. When studies exhibited low heterogeneity, indicated by a P-value for the Q statistic of ≥ 0.1 and an I^2 index ≤ 50%, we utilized a fixed effects model. This model assumes that the studies included in the meta-analysis are estimating the same true effect size, and it provides a single summary estimate. Conversely, for studies demonstrating substantial heterogeneity, we adopted a random effects model. This model acknowledges that the true effect size may vary across studies and thus provides a more conservative estimate, incorporating this variability into the final summary effect. To delve deeper into the sources of heterogeneity observed among the studies, we conducted subgroup analyses. By comparing the results within and between subgroups, we aimed to identify potential factors contributing to the observed heterogeneity. P-value > 0.05 in these tests suggested that there was no significant evidence of bias.

Results

Search results

Flowchart illustrating the selection process is showed in Fig. 1. A total of 210 studies were initially screened across 3 academic research databases. After removing duplicates and inconsistent literature, 4 studies ultimately met the inclusion criteria for the meta-analysis [11–13, 22].

The publication years of the included studies ranged from 2009 to 2018. Three studies (75%) included HD patients and two studies (50%) had keto acids added to a low-protein diet. Most of them were in small sample sizes, ranging from 40 to 142 patients, and follow-up times varied from 4 to 12 + months. Additional details can be found in Table 1.

Quality assessment

Among the two RCTs, only random sequence generation showed a low risk of bias (Fig. 2). Majority exhibited low or unclear risk of bias. We assessed the remaining studies using the NCO scale, with a score of 7.5 for the non-randomized controlled trial and 5 for the prospective observational study. Of the two, Stefania's research on selection of the non-exposed cohort, comparability of cohorts on the basis of the design or the analysis and comparability of cohorts on the basis of the measurement options received higher scores.

Effects of interventions

Residual renal function

Three studies involving a total of 270 patients reported data on residual renal function (RRF) with follow-up at least 12 months.

If data of all durations was combined, a significant difference in GFR was presented within the subgroup of patients following a 12-month low-protein diet (three studies; 270 patients; MD = 1.37 ml/min; 95% CI, 0.18 to 2.55; I^2 = 84%) (Fig. 3A). Subsequently, to address the high heterogeneity, we conducted a subgroup analysis. The subgroup of the 'baseline GFR < 4 ml/min' showed no heterogeneity (I^2 = 0%, P < 0.00001), and the subgroup of the 'baseline GFR ≥ 4 ml/min' demonstrated high heterogeneity (I^2 = 94%, P = 0.39) (Fig. 3B). Consequently, dialysis patients who adhered to a long-term low-protein diet, especially those with a lower baseline GFR, experienced a slower decline in GFR.

Similarly, for daily urine volume, three studies of 270 patients were reported, while follow-up at least 12 months. There was a significant difference in GFR within the subgroup of patients following the 12-month low-protein diet (three studies; 270 patients; MD = 660 ml; 95% CI, 110 to 1210; I^2 = 97%) (Fig. 3C). To address the high heterogeneity, we conducted a subgroup analysis. The subgroup of the 'peritoneal dialysis' presented low heterogeneity (I^2 = 36%, P = 0.07), while the subgroup of the 'hemodialysis' demonstrated high heterogeneity (I^2 = 97%, P = 0.006) (Fig. 3D). Consequently, dialysis patients who adhered to a long-term low-protein diet better retain daily urine volume, especially those undergoing hemodialysis. This suggests that a long-term low-protein diet shows positive influence on dialysis patients' residual renal function.

Nutritive index

The nutritive index was assessed in four studies involving 310 patients, with the follow-up periods ranging from 4 to 12 + months.

Overall, no significant difference in serum albumin levels was observed (MD = 0.40 g/dl; 95% CI, -2.43 to 3.24; I^2 = 90%, P = 0.78). However, subgroup analysis revealed significant differences and low heterogeneity in the 'Control DPI 1.0-1.2 g/kg/d' (I^2 = 21%, P = 0.04) and 'Control free-choice diet' (I^2 = 0%, P < 0.00001) (Fig. 4A).

Serum calcium showed no significant difference (MD = 1.08 g/dl; 95% CI, -1.02 to 3.19; I^2 = 99%, P = 0.31) (Fig. 4B), while a significant difference in serum phosphorus was observed (MD=-0.74 g/dl; 95% CI, -1.04 to -0.45; I^2 = 90%, P = 0.78) (Fig. 4C). By subgroup analysis, both the subgroup of the 'keto acids' (I^2 = 68%, P < 0.0001) and 'no keto acids' (I^2 = 0%, P = 0.001) demonstrated significant difference.

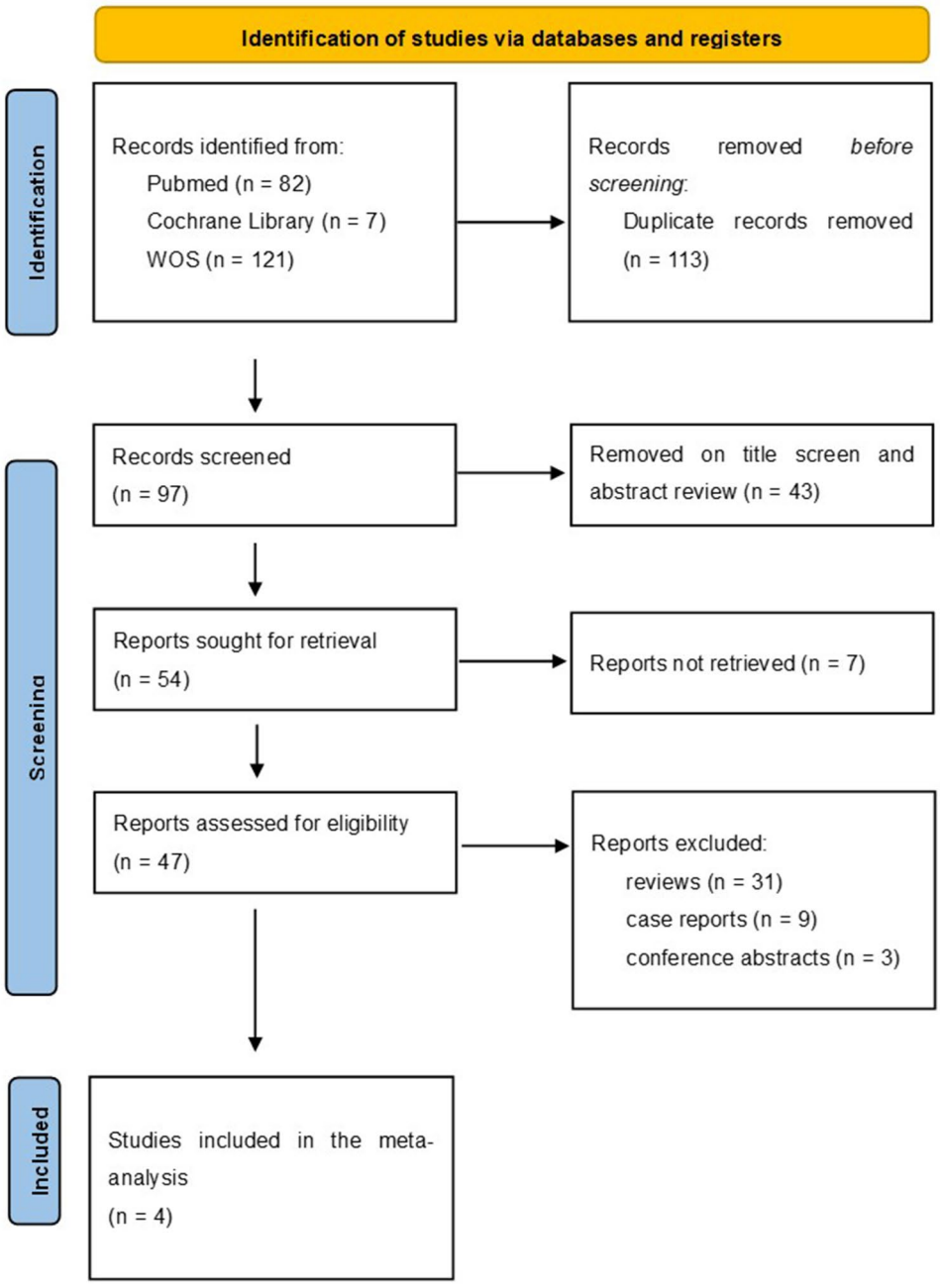

Fig. 1 Flow diagram of articles considered for inclusion

Dialysis patients adhering to a low-protein diet exhibited lower serum albumin levels compared to those adhering to a DPI of 1.0–1.2 g/kg/d diet, but demonstrated higher serum albumin comparing to those adhered to free-choice diet. Besides, whether or not keto acids were added, dialysis patients who adhered to a low-protein diet had lower serum phosphorus levels than others.

Other outcomes

No significant difference was observed among these results: all-cause mortality (RR = 0.55; 95% CI, 0.26 to 1.18; $I^2 = 0\%$, $P = 0.13$) (Fig. 5A), KT/V (MD = 0.05; 95% CI, -0.06 to 0.17; $I^2 = 0\%$, $P = 0.37$) (Fig. 5B), the number of adverse events (infection, cardiovascular event or hospitalization for other reasons) (RR = 0.42; 95% CI, 0.17 to 1.04; $I^2 = 55\%$, $P = 0.06$) (Fig. 5C), and the number of patients who dropped for declining of residual renal function (RR = 0.64; 95% CI, 0.19 to 2.13; $I^2 = 5\%$, $P = 0.47$) (Fig. 5D).

Table 1 Characteristics of the included studies

study	year	country	study design	dialysis	inclusion criteria	sample size	funding source
Na Jiang et al.	2009	China	RCT	PD	GFR≥2 ml/min/1.73 m2, urine output≥800 ml/day	60	non industry
Haiming et al.	2010	China	RCT	HD	Kt/V>1.2, serum phosphorus>5.5 mg/dl	40	non industry
Stefania et al.	2014	Italy	Non-RCT	HD	GFR 5 to 10 ml/min	68	NR
Toshiyuki et al.	2018	Japan	prospective	HD	GFR<5.0 mL/min or Scr>8.0 mg/dL	142	NR

study		sample size	male/female	average age	followup time	PI treatment/control
Na Jiang et al.	treatment group	20	7/13	51.4 ± 13.8	12M	DPI 0.6-0.8 g/kg/day
	treatment group	20	11/9	56.3 ± 11.6	12M	DPI 0.6-0.8 g/kg/day + 0.12 g/kg/day keto acids
	control group	20	12/8	53.0 ± 13.2	12M	DPI 1.0-1.2 g/kg/day
Haiming et al.	treatment group	20	10/10	52.4 ± 84.9	4M	DPI 0.8 g/kg/day + phosphate 500 mg/day+ keto acids
	control group	20	11/9	51.1 ± 85.8	4M	DPI 1.0-1.2 g/kg/day
Stefania et al.	treatment group	38	25/13	64.5 ± 13.2	12M	DPI 0.6 g/kg/d
	control group	30	19/11	65.2 ± 11	12M	free-choice diet
Toshiyuki et al.	treatment group	112	80/42	63 ± 6	12M+	DPI 0.6 g/kg/d + less than 6 g/day of salt intake
	control group	30	NR	NR	NR	free-choice diet

NR: not report.

Discussion

This systematic review and meta-analysis showed that long-term adherence to a low-protein diet has a positive impact on dialysis patients' residual renal function.

We observed improvements in both GFR and daily urine volume in dialysis patients after 12 months of adherence to a low-protein diet, which is particularly significant for patients with low baseline GFR and those undergoing hemodialysis. With the intervention of low-protein diet, the renal function of these patients has been protected and improved to a certain extent. By restricting protein intake [8, 23], DPI 0.6–0.8 g/kg/day effectively minimizes the production of nitrogen waste, thus alleviating the metabolic stress on the kidneys. It diminishes the likelihood of glomerular sclerosis and fibrosis to slow down the deterioration of renal function. Moreover, low-protein diet potentially exerts a positive impact on the kidneys by modulating inflammatory factors and rectifying acid-base imbalances as well as electrolyte disturbances [7, 24]. Its benefits collectively contribute to the preservation of kidney health and slow the progression of any existing kidney ailments.

In addition, our findings indicate that the addition of keto acids had not significant effect on dialysis patients' residual renal function, who following a low-protein diet through heterogeneity analysis. But in studies of CKD patients, ketone analogues of essential amino acids can trap excess nitrogen residues for essential amino acid production to reduce the formation of endogenous urea [25]. For CKD patients, supplementation with the low-protein diet and ketoacids can effectively ameliorate metabolic disorders, reduce the rate of kidney function decline, and delay the initiation of dialysis without any negative impact on nutritional status [26–31]. Supplemented with keto acids has no additional benefit may be related to dietary adherence [31]. More relevant clinical studies on dialysis patients are needed to explain this phenomenon.

While a low-protein diet exhibits a positive impact on dialysis patients' residual renal function, prolonged

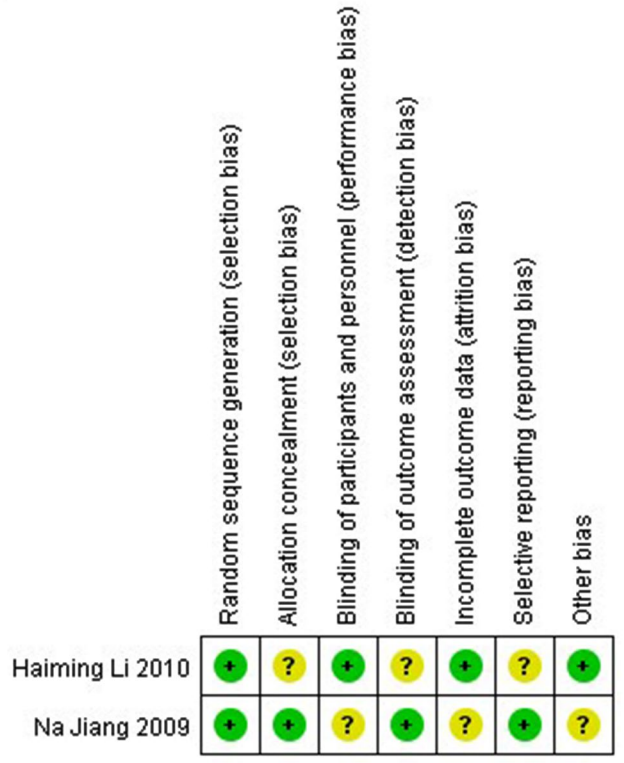

Fig. 2 Risk of bias summary: review authors' judgements about each risk of bias item for RCTs

adherence to such a diet may pose certain risks like the change of serum electrolytes, malnutrition and compromised immunity [14–16]. Our comprehensive study revealed dialysis patients adhering to a low-protein diet exhibited lower serum phosphorus levels and relatively high serum albumin concentrations, indicating a favorable nutritional status. We observed no alterations in serum calcium levels, which aligns with the findings of a meta-analysis involving patients with kidney disease [32] and warrants further interpretation in additional studies. High levels of phosphoric acid associated with increased mortality and cardiovascular disease pose a risk to dialysis patients [33]. Phosphorus intake is closely related to protein [12] and a low-protein diet can slow down serum phosphoric acid levels. While a high serum albumin concentration indicates good nutritional status [34]. This underscores the necessity of meticulously monitoring these patients' nutritional status and promptly adjusting their dietary regimens. It ensures that dialysis patients with a low-protein diet receive adequate nutritional support and minimizes the potential risks associated with long-term dietary restrictions while maximizing the protective benefits for their residual renal function [26, 35, 36]. A low protein diet of 0.6 g/kg/day can reduce the accumulation of nitrogenous waste products [37] and may also prevent negative nitrogen balance, which is reflected in the improvement of albumin and phosphorus levels. At present, it appears that low-protein diets have a certain level of safety, and with personalized diets and long-term monitoring [38], malnutrition may not occur.

Although the protective impact of a low-protein diet on dialysis patients' residual renal function has been demonstrated, there are differences in the tolerance of low-protein diets among dialysis patients. We observed no significant difference in this meta-analysis, but in a study which was not included for lack of a control group [13], 27 of 112 hemodialysis patients dropped out of a low-protein diet due to decreased renal function in 12

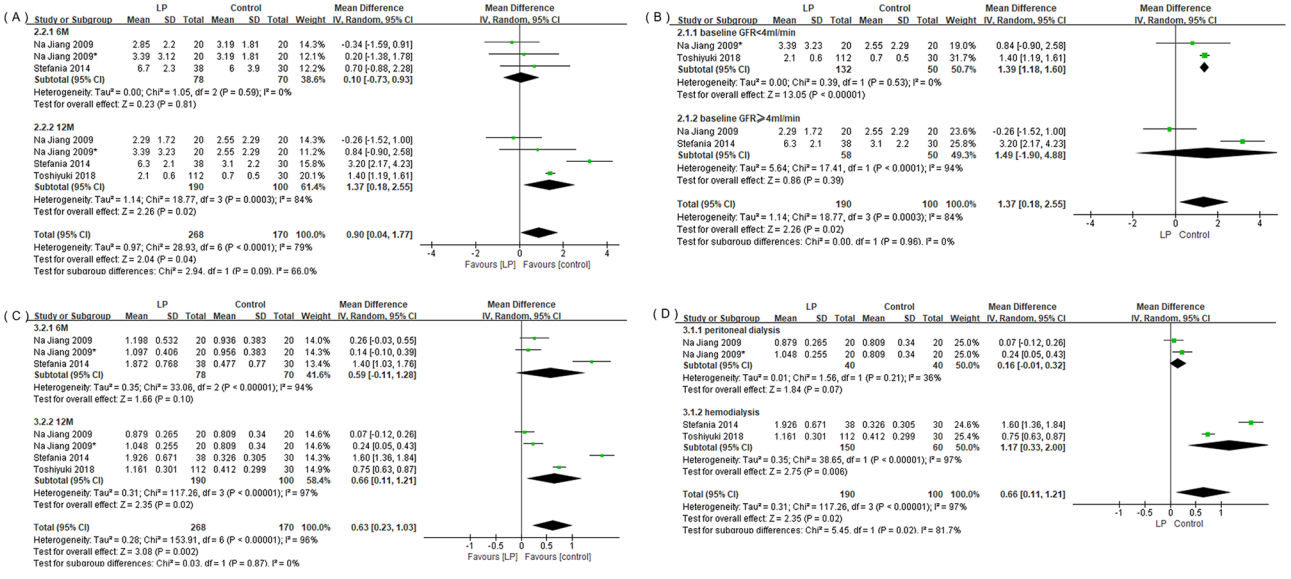

Fig. 3 Forest plots of residual renal function in dialysis patients. (**A**) GFR for all durations; (**B**) GFR for patients following a 12-month low-protein diet; (**C**) daily urine volume for all durations; (**D**) daily urine volume for patients following a 12-month low-protein diet. *: low protein diet with keto acids added

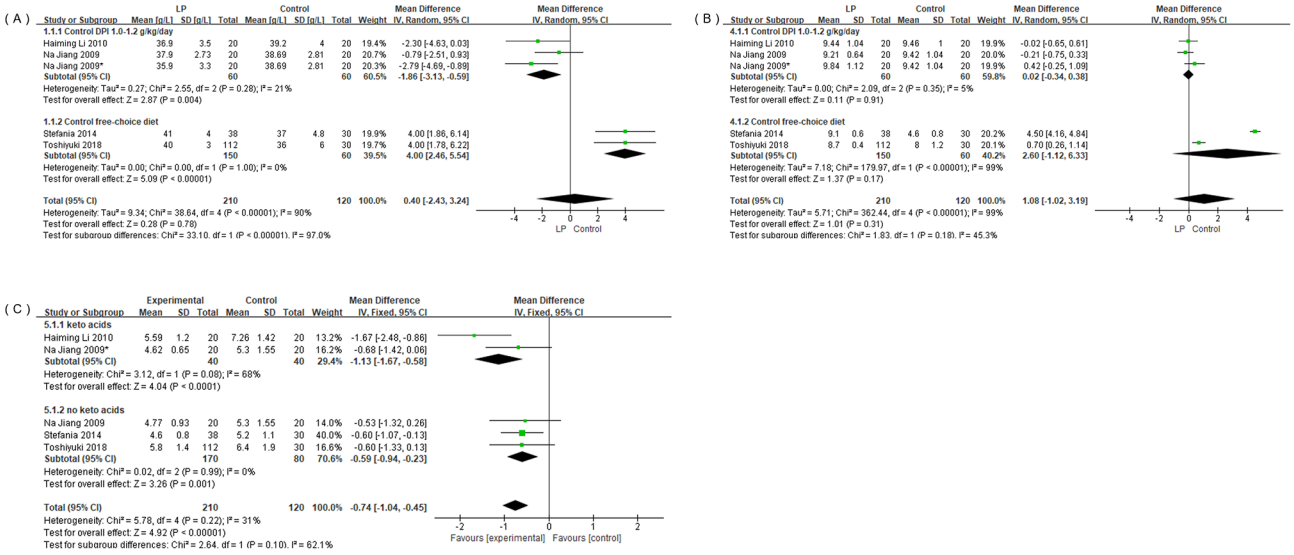

Fig. 4 Forest plots of nutritive index in dialysis patients. (**A**) serum albumin; (**B**) serum calcium; (**C**) serum phosphorus. *: low protein diet with keto acids added

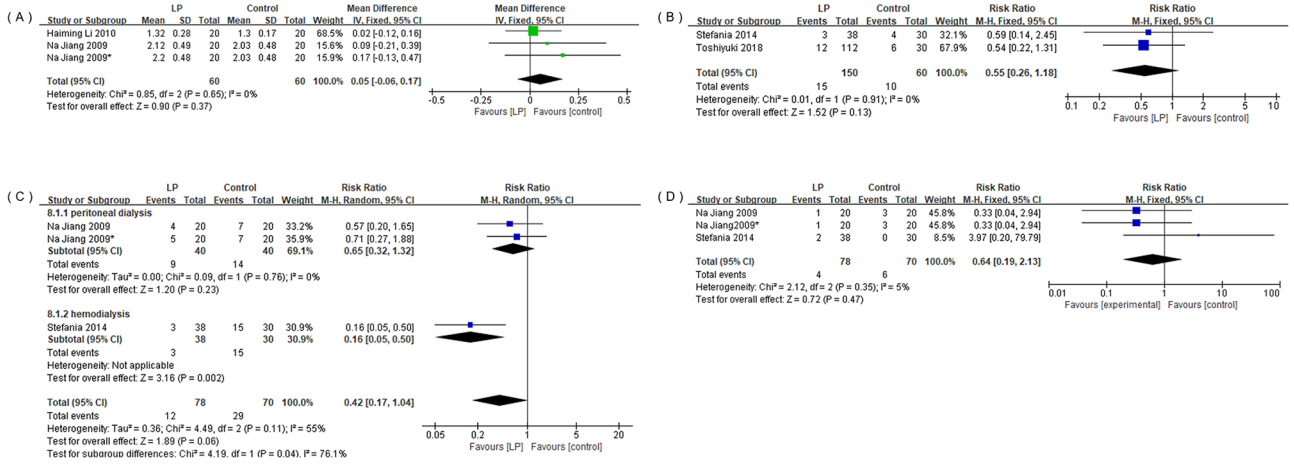

Fig. 5 Forest plots of other outcomes in dialysis patients. (**A**) all-cause mortality; (**B**) KT/V; (**C**) the number of adverse events; (**D**) the number of patients dropped for declining of residual renal function. *: low protein diet with keto acids added

months. It may be that the mode of dialysis affects the tolerance of patients following a low-protein diet. For peritoneal dialysis [3, 39], peritoneum serves as a semi-permeable membrane, facilitating solute exchange and water clearance between blood and peritoneal permeable fluid within the peritoneal capillaries. As peritoneal dialysis patients exhibit a relatively lower reliance on residual renal function [40], they often maintain a good tolerance to a low-protein diet even as renal function diminishes [41]. Contrastingly, hemodialysis involves the artificial establishment of a cardiopulmonary bypass system, where blood is circulated through a dialysate for the purpose of substance exchange [42]. This process aims to eliminate waste products and excess water from the body, making hemodialysis patients more dependent on residual renal function [41]. As a result, when renal function deteriorates, hemodialysis patients may encounter greater challenges in maintaining a low-protein diet.

Since patients differ in renal function, dialysis methods, and nutritional status, it's particularly essential to develop a personalized diet plan [43]. Strengthening patient education and nutritional counseling can help reduce complications and adverse consequences due to improper diet [36]. Furthermore, studying the optimal protein intake level to balance kidney protection and nutritional adequacy is also an important research direction. This will help us to develop a more scientific and rational diet management program for dialysis patients.

Although our study has achieved these results, there are still some limitations. First, the number of included studies was limited, which may affect the stability and reliability of the results. Some studies were excluded due

to copyright restrictions, paywalls, absence of control group and insufficient data on kidney function. Besides, there has been a greater focus on conducting clinical trials involving patients with predialysis CKD, while fewer have been conducted on those undergoing dialysis. Second, potential publication bias may also have an impact on the results. In addition, the high degree of heterogeneity observed in some analyses may also pose difficulties in the interpretation of the results. These limitations suggest that when interpreting and using the results of this study, we should be cautious and conduct a comprehensive analysis in conjunction with other relevant studies. Larger randomized controlled trials are in need to further verify the protective impact of a low-protein diet on dialysis patients' residual renal function, explore the long-term influence, and investigate the variations in effects among patients using different dialysis modalities.

Conclusion

In summary, this study evaluated the influence of a low-protein diet on dialysis patients' residual renal function through a systematic review and meta-analysis. The results showed that adherence to a low-protein diet for 12 months had positive effects on residual renal function and nutritional status of dialysis patients. Future research should delve deeper into the optimal practices for low-protein diets and their long-term effects on managing dialysis patients. Through further research with larger sample and the implementation of a personalized diet plan, it may be possible to balance the need for kidney protection with adequate nutrition and improve patients' quality of life.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12882-025-04042-1.

Supplementary Material 1

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Author contributions
Jingyi Xie and Xiaoqin Liu analyzed data and wrote the manuscript. Shuwang Ge and Ying Yao substantively revised the manuscript. All authors read and approved the final manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

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Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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