How to optimize nutritional care in patients with CKD?

Speaker:
Laetitia Koppe,
France

Panellist:
Stephan Bakker,
The Netherlands

Panellist:
Andrew Davenport,
UK

Moderator:
Giuseppe Castellano,
Italy

Chronic kidney disease (CKD) is projected to affect an increasing number of individuals globally related to the ageing of the population. Adequate nutrition is an integral component of CKD management as it may help preserve renal function and prevent the complications, such as protein-energy wasting (PEW) and uremic symptoms. Furthermore, nutritional status is associated with morbidity, mortality, functional activity and quality of life in CKD patients. Hence, careful monitoring of nutritional status and optimization of nutritional care is essential in this population and requires active involvement from renal dietitians.

Current recommendations for protein intake in CKD patients

The recent KDOQI Clinical Practice Guidelines for Nutrition in CKD: 2020 Update provide comprehensive and up-to-date information on nutritional care in the CKD population for practicing clinicians and allied health-care workers. The guideline was developed as a joint effort by the National Kidney Foundation and the Academy of Nutrition and Dietetics to address adult CKD patients in stages 1 through 5, including patients on maintenance dialysis and those with a kidney transplant. They clearly outline nutritional assessment recommendations. This UpToDate extend guidance to medical nutrition therapy, nutritional supplementation, micronutrients and electrolytes, which are now incorporated as standalone sections.

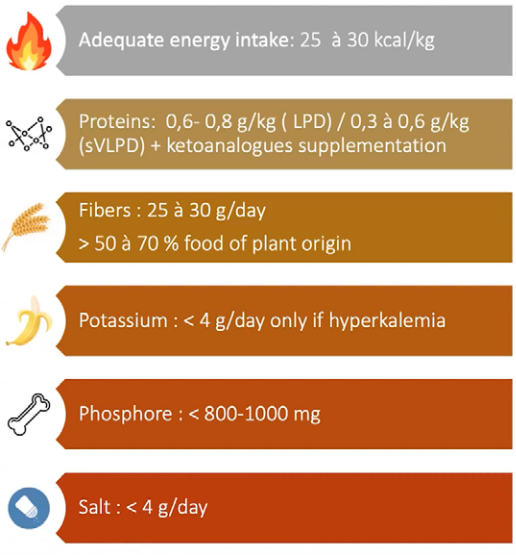

Figure 1.
Summary of 2020 KDOQI Nutritional Guidelines for CKD patients

One important point in the current guidelines is the recommended protein intake for non-dialysis patients. The modification introduced in this area was based on a substantial number of studies published over the last two decades that provided a more comprehensive analysis of the effectiveness of protein restriction on CKD progression, with or without keto-acid analogues supplementation. Specifically, the updated statements highlight that the low- (0.55 – 0.6 g/kg/day) or very low (0.28 – 0.43 g/kg/day with keto-acid analogues) protein diets are adequate for nondiabetic and metabolically stable patients with stages 3B-5 CKD. Given the lack of specific studies, patients with diabetic kidney disease may have more modest protein restriction (0.6 – 0.8g/kg/day). This particular recommendation has raised much debate that is still ongoing. It is argued that even though it appears to be relying on strong evidence of beneficial effects, such severe protein restriction might also impose a substantial burden on the patients, possibly forcing them to significantly alter their cultural norms, separate from communal meals and experiences and potentially reduce their quality of life for an assumed minor benefit that would potentially become apparent only after decades of maintaining such regimen.

The rationale for low-protein intake in CKD patients

The effects of protein intake on renal function and structure have been broadly investigated and discussed in the nephrology community for decades. A recent meta-analysis of randomized controlled trials in adult, non-diabetic, non-dialysis-dependent patients aimed to assess the efficacy of low-protein diets in preventing the natural progression of CKD and delaying dialysis treatment. It identified 17 studies (21 separate data sets) with nearly 3,000 patients, executed from 1984 to 2013, with a mean follow-up ranging from 12 to 50 months. Ten studies compared a low-protein diet with a normal protein intake, eight compared a very low-protein diet with a low-protein diet, and two compared a very low-protein diet with a normal protein intake. The overall conclusion was that very low-protein diets probably reduce the number of patients with CKD 4 or 5 who progress to end-stage renal disease (ESRD), while low-protein diets do not exhibit such remarkable effects. No data was found on the impact of dietary protein restriction on patients' quality of life, and data on weight changes and protein energy wasting were limited. A more recently published prospective observational study by Metzger et al. corroborated these findings by observing a significant association between lower dietary protein intake (assessed from 24-hour urinary urea excretion or by dietary interview) and slower CKD progression. Also, current evidence suggests that a low-protein diet mitigates proteinuria, probably related to the reduction of intraglomerular pressure independently or/and synergistically of angiotensin-pathway modulation.

More recent research has gone even further in elucidating the impact of protein intake on kidney function related to the latest advances in understanding the diet-microbiota crosstalk in the uremic context. Namely, besides being metabolized to urea in the liver, dietary proteins are also processed by the gut microbiota into metabolites that may have a deleterious effect on kidney functions (such as trimethylamine N-oxide –TMAO–, p-cresyl sulfate, and indoxyl sulfate from the fermentation of amino acids). Therefore, restricting dietary protein results in a proportional reduction in urea generation, and parallel reductions of other nitrogenous compounds acting as uremic toxins, especially indoxyl sulfate and p-cresyl sulfate. It may also modify gut microbiota composition and associated inflammatory and metabolic parameters in CKD patients.

Open issues with low-protein intake dietary regimens

Common concerns associated with the employment of low-, and especially very-low protein diets, are the risks of malnutrition and low muscle mass. Nevertheless, several studies presented reassuring evidence that both low- (0.55 – 0.80g/kg/day) and supplemented very-low (0.3 – 0.4g/kg/day) protein diets are safe

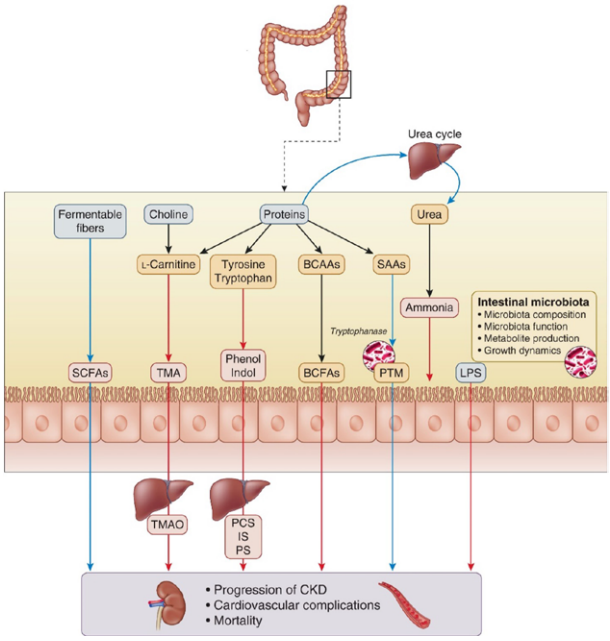

Figure 2.
The pathway linking dietary intake, gut microbiota and kidney disease progression (from Koppe et al, KI, 2022)

for clinically stable patients with CKD stages 3-5, provided that the energy intake is adequate. Namely, it has been observed that, in the short term, patients successfully adapt to low protein intakes and maintain a neutral, or even slightly positive nitrogen balance. It is important to emphasize that the concept of "adaptation" to low protein intakes is very far from the concept of "accommodation," the latter term implying a decrease in protein synthesis, with the development of wasting when inadequate dietary protein intake overcomes the limits of the adaptive mechanisms. Thus, protein-energy wasting is more related to protein degradation and/or decreased synthesis related to insulin/IGF-I resistance, acidosis and chronic inflammation than with low protein intake. Finally, recent long-term randomized clinical trials on supplemented very-low protein diets in CKD patients presented a very favourable safety profile, suggesting that observations in short-term studies on muscle protein turnover can be extrapolated to the long-term period.

Recent expert discussions also focused on the sources of dietary proteins for CKD patients. A recent study suggested that red meat increases the risk of ESRD, while the same was not observed related to poultry, fish, eggs or dairy products. Actually, substituting one serving of red meat with other sources of protein significantly reduced the risk of ESRD. The possible explanations include greater acid production related to red meat consumption compared to other animal-source proteins, and the roles of nitrites, nitrates, heme iron, advanced glycation end-products,

lipoxidation end-products and TMAO production. Animal studies have also shown that reducing the aromatic amino-acid load (namely low intake of tyrosine, tryptophan and phenylalanine) in a normoproteic diet may have a similar beneficial effect on CKD progression as a low-protein diet. A similar beneficial effect was seen in animal models with increasing the amount of sulfur amino acids, methionine and cysteine, in a normoproetic diet. All of this suggest that the composition of amino acids is important for the nephroprotection.

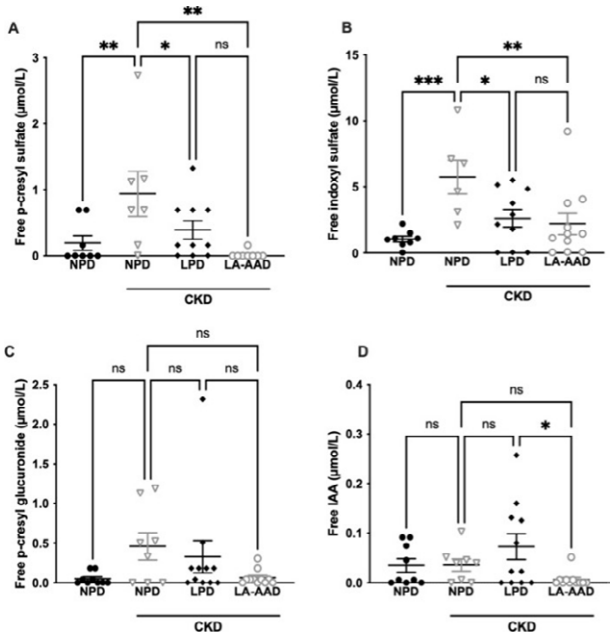

Figure 3.
Effects of normoproetic diet (NPR), low-protein diet (LPD) and low aromatic amino-acid diet (LA-AAD) on the levels of certain uremic toxins in control and CKD mice

Dietary fibres and CKD

Many studies underline the beneficial effects of high fibre intake on decreasing inflammation and mortality risk in the general population and CKD patients. Furthermore, fibre-rich diets reduce constipation which is commonly present in the CKD population and is associated with increased cardiovascular risk (probably through processes mediated by altered microbiota), inflammation, progressive eGFR decline and diminished quality of life. Plant nutrients and plant-based diets are excellent sources of fibres, and organic and non-organic bases, and several large observational studies reported a positive association between higher adherence to plant-based diets and favourable kidney disease outcomes. Among the numerous beneficial effects of these types of diets in CKD patients are shifting the gut microbiota towards reduced production of uremic toxins due to increased fibre intake, antiatherogenic effects from plant fats, mitigating metabolic acidosis, and improved control of hyperphosphatemia since plant phosphorus has a lower bioavailability than animal phosphorus. Unfortunately, patients often find it challenging to meet the recommendations for adequate fibre intake because of the lower intake of fruits and vegetables related to imposed potassium restrictions. Still, recent data suggest insufficient proof for the association between oral potassium intake and serum potassium levels, thus suggesting consideration of a more flexible attitude to dietary potassium restriction in CKD patients which might also contribute to a more suitable fibre intake.

Future considerations

Although diet is the cornerstone of the management of patients with CKD, it remains underused in everyday clinical practice. More data is still needed on the diet-gut microbiota-metabolite interactions, the impact of selected biotics and bioactive compounds, types of food processing and patient-related parameters on morbidity, mortality, kidney function, quality of life and other functional symptoms. There is emerging evidence that certain dietary supplements, such as amino acids, proteins, ginseng, red ginseng and herbal medicine berries are associated with a higher prevalence of CKD; while probiotic supplements may have beneficial effects on renal function. Therefore, future studies should explore the exact effects of each dietary supplement on CKD. Finally, given the acknowledged importance of nutritional management in CKD, more efforts should be invested in implementing consistent, specialized renal dietary counselling in the regular management of CKD patients.

Writen by: Jasna Trbojevic-Stankovic
The speaker reviewed and approved the content.

KEY POINTS

1. Low-and very-low protein diets have been recommended for non-diabetic and metabolically stable patients with stages 3 and 4 CKD based on their beneficial effects on renal function preservation.

2. Dietary protein restriction reduces the production of nitrogenous uremic toxins (indoxyl sulfate, p-cresyl sulfate).

3. Low-protein intake may also modify gut microbiota composition and associated inflammatory and metabolic parameters in CKD patients.

4. Fiber-rich diet alleviates constipation, decreases inflammation and improves cardiovascular and renal prognosis in CKD patients.

5. Plant-based dietary regimens provide adequate fibre intake, reduce uremic toxins production, mitigate metabolic acidosis and improve phosphatemia control.

6. Regular specialized nutritional counselling should be endorsed as an integral part of CKD management.

Further readings

1. Ikizler TA, Burrowes JD, Byham-Gray LD, et al. KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update [published correction appears in Am J Kidney Dis. 2021 Feb;77(2):308]. Am J Kidney Dis. 2020;76(3 Suppl 1):S1-S107. doi:10.1053/j.ajkd.2020.05.006
2. Obeid W, Hiremath S, Topf JM. Protein Restriction for CKD: Time to Move On. Kidney360. 2022;3(9):1611-1615. doi:10.34067/KID.0001002022
3. Kalantar-Zadeh K, Fouque D. Nutritional Management of Chronic Kidney Disease. N Engl J Med. 2017;377(18):1765-1776. doi:10.1056/NEJMra1700312
4. Koppe L, Soulage CO. The impact of dietary nutrient intake on gut microbiota in the progression and complications of chronic kidney disease. Kidney Int. 2022;102(4):728-739. doi:10.1016/j.kint.2022.06.025
5. Metzger M, Yuan WL, Haymann JP, et al. Association of a Low-Protein Diet With Slower Progression of CKD. Kidney Int Rep. 2017;3(1):105-114. Published 2017 Aug 30. doi:10.1016/j.ekir.2017.08.010
6. Hahn D, Hodson EM, Fouque D. Low protein diets for non-diabetic adults with chronic kidney disease. Cochrane Database Syst Rev. 2020;10(10):CD001892. doi:10.1002/14651858.CD001892.pub5
7. Marzocco S, Dal Piaz F, Di Micco L, et al. Very low protein diet reduces indoxyl sulfate levels in chronic kidney disease. Blood Purif. 2013;35(1-3):196-201. doi:10.1159/000346628
8. Di Micco L, Di Lullo L, Bellasi A, Di Iorio BR. Very Low Protein Diet for Patients with Chronic Kidney Disease: Recent Insights. J Clin Med. 2019;8(5):718. doi:10.3390/jcm8050718
9. Lin PC, Chou CL, Ou SH, Fang TC, Chen JS. Systematic Review of Nutrition Supplements in Chronic Kidney Diseases: A GRADE Approach. Nutrients. 2021;13(2):469. doi:10.3390/nu13020469
10. Garibotto G, Picciotto D, Saio M, Esposito P, Verzola D. Muscle protein turnover and low-protein diets in patients with chronic kidney disease. Nephrol Dial Transplant. 2020;35(5):741-751. doi:10.1093/ndt/gfaa072
11. Lew QJ, Jafar TH, Koh HW, et al. Red Meat Intake and Risk of ESRD. J Am Soc Nephrol. 2017;28(1):304-312. doi:10.1681/ASN.2016030248
12. Barba C, Benoit B, Bres E, et al. A low aromatic amino-acid diet improves renal function and prevent kidney fibrosis in mice with chronic kidney disease. Sci Rep. 2021;11(1):19184. doi:10.1038/s41598-021-98718-x
13. Krishnamurthy VM, Wei G, Baird BC, et al. High dietary fiber intake is associated with decreased inflammation and all-cause mortality in patients with chronic kidney disease. Kidney Int. 2012;81(3):300-306. doi:10.1038/ki.2011.355
14. Carrero JJ, González-Ortiz A, Avesani CM, et al. Plant-based diets to manage the risks and complications of chronic kidney disease. Nat Rev Nephrol. 2020;16(9):525-542. doi:10.1038/s41581-020-0297-2
15. Gutiérrez OM, Muntner P, Rizk DV, et al. Dietary patterns and risk of death and progression to ESRD in individuals with CKD: a cohort study. Am J Kidney Dis. 2014;64(2):204-213. doi:10.1053/j.ajkd.2014.02.013
16. Kim H, Caulfield LE, Garcia-Larsen V, et al. Plant-Based Diets and Incident CKD and Kidney Function. Clin J Am Soc Nephrol. 2019;14(5):682-691. doi:10.2215/CJN.12391018
17. Kim H, Caulfield LE, Garcia-Larsen V, et al. Plant-Based Diets and Incident CKD and Kidney Function. Clin J Am Soc Nephrol. 2019;14(5):682-691. doi:10.2215/CJN.12391018
18. Sumida K, Molnar MZ, Potukuchi PK, et al. Constipation and Incident CKD. J Am Soc Nephrol. 2017;28(4):1248-1258. doi:10.1681/ASN.2016060656
19. De Nicola L, Garofalo C, Borrelli S, Minutolo R. Recommendations on nutritional intake of potassium in CKD: it's now time to be more flexible!. Kidney Int. 2022;102(4):700-703. doi:10.1016/j.kint.2022.04.046
20. Ma Y, He FJ, Sun Q, et al. 24-Hour Urinary Sodium and Potassium Excretion and Cardiovascular Risk. N Engl J Med. 2022;386(3):252-263. doi:10.1056/NEJMoa2109794
21. Fang Y, Lee H, Son S, et al. Association between Consumption of Dietary Supplements and Chronic Kidney Disease Prevalence: Results of the Korean Nationwide Population-Based Survey. Nutrients. 2023;15(4):822. doi:10.3390/nu15040822