

Chronic Kidney Disease

Protein requirements



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This article focuses on the current evidence around estimating protein requirements in people with chronic kidney disease (CKD). The article is divided into two parts. The first will focus on low protein diets in CKD, specifically in the outpatient/community settings, reviewing the recent evidence. The use of dietary approaches to influence metabolic acidosis, plant and Mediterranean diets in CKD are outside the scope of this article and will only be briefly mentioned. The second part will focus on protein provision in patients with CKD while they are either admitted to hospital with or without an acute illness. The article reflects the opinion of the author only and is based on his critical appraisal of the related evidence base and his practical experience of working with people with CKD.

Terminology & practical consideration

Universal definitions of low protein diets do not exist. As a result, different guidelines, systematic reviews, meta-analysis and randomised controlled trials (RCT) use their own definitions for a very low protein diet, low protein diet and 'normal' protein diet. Some authors define a low protein diet as less than 0.6 g protein/kg/body weight (BW)/day and a very low protein diet as less than 0.4 g protein/kg/BW/day.¹ Others define low protein diets as less than 0.8 g protein/kg/BW/day. For example, a 2018 systematic review and meta-analysis showed that a low protein diet (using less than 0.8 g protein/kg/BW/day) can be considered for people with CKD who opt for conservative management, posing only a minimal risk of cachexia or protein energy wasting.² When reviewing the literature in relation to a low protein diet and CKD, it is important to be familiar with the terminology used and be aware of the differing definitions of what constitutes as a 'low protein diet'.

In addition, many guidelines provide recommendations based on grams (g) of protein per kg of either actual or ideal body weight (IBW). Most of the recommendation of 'g of protein/kg/BW/day' are not applicable to people at the extremes of body mass index (BMI) - e.g. underweight, overweight and obese people with CKD. Furthermore, estimating IBW methodologies remain poorly defined. Although, to assist,

the British Dietetic Association (BDA) Parenteral and Enteral Nutrition Specialist Group (PENG) have produced a consensus statement on IBW: <https://bit.ly/PENGIBW>.

Protein requirements in CKD

Low protein diets in patients with CKD have been (and still are) a subject of debate within the clinical nephrology and renal dietetics communities, with some enthusiastic supporters and other sceptical clinicians. As a result, there are guidelines which differ significantly on their recommendations, contradicting each other and often causing confusion not only for the clinicians but also for people with kidney disease. **Table 1** summarises the key guidelines and reviews from 2000, demonstrating the changes in the past 20 years.

In 2000, the Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines recommended a protein provision of 0.6 g/kg/BW/day in people with CKD stage 4 and 5, offering a relaxed approach up to 0.75 g protein/kg/BW/day for those who struggled to meet 0.6 g/kg/BW/day.¹ These guidelines were mainly based on the Locatelli study conducted in 1991,¹¹ where they randomised 456 adult patients to either a 0.6 g/kg/BW/day (n=226) or a 'normal' 1 g/kg/BW/day (n=230). The study failed to achieve a statistical significance (p value of 0.06), yet the study was interpreted as being favourable towards a low protein diet.¹¹

Table 1: Protein requirement recommendations – 2000-2022

	eGFR ml/min per 1.73m ²	People with diabetes	People without diabetes
KDOQI 2000 ¹	<25 ml/min		<0.6 g protein/kg/BW/day If not tolerated 0.75 g protein/kg/BW
Cochrane Review 2007 ³	Moderate to severe <30 ml/min	More research needed as compliance to a low protein diet was not achieved (intake was 0.7-1.1 g/protein/kg/BW/day)	N/A
Cochrane Review 2009 ⁴	Moderate to severe <30 ml/min	N/A	Reducing protein intake in patients with CKD reduces the occurrence of renal death by 32% when compared with higher or unrestricted protein intake. The optimal level of protein intake cannot be confirmed from these studies.
KDIGO Guidelines 2012 ⁵	<30 ml/min		0.8 g/kg/BW/day avoid >1.3 g/kg/BW/day in people at-risk of progression
UKKA 2019, endorsed by RNG ⁶	<30 ml/min	0.8-1.0 g/kg/ideal BW/day	
KDOQI 2020 ⁷	<60 ml/min	0.6-0.8 g/kg/BW/day (opinion)	In adults with CKD 3-5 who are metabolically stable, we recommend under close supervision protein restriction with or without keto analogues, to reduce the risk of ESKD/death (1a) and Improve QOL (2c): <ul style="list-style-type: none"> • 0.55-0.6 g/kg/BW/day or • 0.28-0.43 g/kg/BW/day + keto acid/amino acid analogue.
Cochrane – Meta-analysis 2020 ⁸	<30 ml/min	N/A	Very low protein diet may reduce ESKD progression. No data on QOL. Studies on QOL are needed before implementation of very low protein diet.
KDIGO 2020 ⁹	(unclear) <60 ml/min	0.8 g/kg/BW/day	N/A
NICE 2021 Guidelines ¹⁰	(unclear) <60 ml/min	Do not offer low protein diet, dietary intake less than 0.6-0.8 g/kg/BW/day to adults with CKD.	

Notes: Level of estimated glomeruli filtration rate (eGFR) and diabetes status distinction stated where applicable. Key: BW = body weight; ESKD = end stage kidney disease; QOL = quality of life.

In 2007 and 2009, the Cochrane Group reviewed the evidence of a low protein diet in people with CKD by their diabetes status. This was the first time that the evidence for low protein diet was divided by the presence or absence of diabetes. The two independent reviews showed that the quality of the evidence was poor in people with CKD and diabetes³ and in those with CKD without diabetes, a reduction of death was observed in the low protein group, but the optimal protein intake could not be identified from those studies.⁴

Since then, a pragmatic approach of 0.8 g protein/kg/BW/day has been adopted in the UK and this was further confirmed in 2012 by the Kidney Disease Improve Global outcomes (KDIGO)⁵ and, in 2019, by the UK Kidney Association (UKKA) guidelines, endorsed by the Renal Nutrition Group (RNG)⁶ and used up until the KDOQI 2020 publication, which 'surprised' the world of renal dietetics by reopening this debate. The KDOQI 2020 guidelines⁷

provide protein recommendation based on diabetes status, replicating what the Cochrane reviews had previously done. In people with diabetes, they suggest 0.6-0.8 g protein/kg/BW/day and they grade this recommendation as 'opinion'.¹ In the same year (2 months later), the KDIGO guidelines for diabetes management in CKD were also published.⁹ They recommended a protein provision of 0.8 g protein/kg/BW/day. Both recommendations (KDOQI¹ and KDIGO 2020⁹) are graded as 'opinion' and, in practical terms, they do both agree that protein intake should not exceed 0.8 g/kg/body weight in people with CKD stage 3-5 and diabetes. Interestingly, the same target has also been recently proposed for people with early stages of diabetic kidney disease (stage 1-3 CKD), as per a recent systematic review and meta-analysis conducted by Li and colleagues in 2021.¹²

Without a doubt the topic of the most discussion, following the publication of the KDOQI 2020 guidelines for nutrition,¹

has been their recommendation for protein provision in patients without diabetes. KDOQI suggest that for adults with CKD stage 3-5, who are metabolically stable and under close supervision, a protein restriction with or without keto analogues to reduce the risk of end stage kidney disease (ESKD)/death (1a) and improve quality of life (QOL) (2c).¹ This can be achieved by either providing diet of 0.55-0.6 g/kg/BW/day or 0.28-0.43 g/kg/BW/day + keto acid/amino acid analogue.¹ What has been received with surprise by many, including the author of this article, is the level of evidence for both reducing the progression of ESKD/death graded as 1a (the highest level of evidence) as well as improving QOL, graded as 2c. The guidelines¹ state: '*In adults with CKD, 5 RCTs reported findings on the effect of protein restriction on survival/deaths. Three studies clearly indicated a beneficial effect of moderate restriction in dietary protein on the development of ESKD/death.*'¹

Let's have a look at these 3 RCTs. The first RCT was the Locatelli study in 1991,¹¹ mentioned earlier in this article. This study has been described as 'borderline significant' in favour of the low protein diet group. However, statistically speaking, a result of $p = 0.06$ is not statistically significant. The second RCT was by Hansen and colleagues in 2002.¹² What really surprised the author of this article was that they used a study that included people with diabetes¹³ to support a claim for people with CKD without diabetes. The third RCT was from Cianciaruso and colleagues, where they randomised 423 patients with CKD 4-5 to either 0.55 g/kg/BW/day or 0.8 g/kg/BW/day. After 32 months, there was no effect on any of the outcomes, protein-caloric malnutrition, dialysis, death, or the composite outcome of dialysis and death.¹⁴ Furthermore, the KDOQI 2020 guidelines stated that '*...pooled together, results from the secondary analysis of the number of events of death/ESKD combined from the 3 RCT indicated a beneficial effect of protein restriction on death/ESKD (OR, 0.621; 95% CI, 0.391-0.985)*'.¹ It is surprising that the KDOQI 2020 guidelines focus their high-level recommendation based on these 3 RCTs, and the author of this article struggles to understand why the Modification of Diet in Renal Disease (MDRD) RCT was not included with these 3 RCTs.¹⁵ The MDRD study clearly did not show any difference in eGFR decline.¹⁵ In addition, no recent RCTs were included in the KDOQI 2020 to support the strong recommendation, meaning that the most recent RCT used in these high-grade recommendations is over 10 years old.

Overall, it is the opinion of the author of this article that the grading level of '1a' is probably overstating the evidence. This is also supported by other authors, such as Obeid and colleagues, who recently produced a short critical appraisal of the KDOQI 2020 nutritional guidelines.¹⁶ Obeid and colleagues also described that it may not just be the quantity but the quality of protein that could have an effect on kidney function, and that adherence to a low protein diet is not easy, especially long-term.¹⁶

There are other aspects that are likely to have an impact on kidney function. For example, the underlying co-morbidities, causes of CKD, medication and many more. Nutritionally, there has been a shift towards limiting dietary acid load and increasing dietary alkali (i.e. fruit

and vegetables) in patients with CKD, especially those at risk of progression;^{1, 17, 18} with some RCT providing encouraging results.¹⁸ For example, in 2019, Garaya *et al.*¹⁸ showed that a regular intake of fruit and vegetables achieved the same results as sodium bicarbonate therapy in treating metabolic acidosis in the early stages of CKD.¹⁸ Moreover, there is a focus on plant-based diets, whole plant-based food and the promotion of the Mediterranean diet, although large RCTs are currently lacking.¹⁹⁻²²

Finally, medical treatment for people with and without diabetes and CKD are changing, especially since the introduction of sodium-glucose cotransporter-2 inhibitors. Therefore, reviewing old and very old RCTs does come with some additional limitations, which should be considered when developing and grading recommendation in new guidelines.

A Cochrane review in 2020⁸ looked at the evidence of a low protein diet in patients with CKD without diabetes. They concluded: '*that very low protein diets probably reduce the number of people with CKD 4-5, who progress to ESKD. In contrast, low protein diets may make little difference to the number of people who progress to ESKD. Low or very low protein diets probably do not influence death. However, there are limited data on adverse effects such as weight differences and protein energy wasting. There are no data on whether quality of life is impacted by difficulties in adhering to protein restriction. Studies evaluating the adverse effects and the impact on quality of life of dietary protein restriction are required before these dietary approaches can be recommended for widespread use.*'⁸ This contradicts the 2020 KDOQI Guidelines.¹

The 2021 National Institute for Health and Care Excellence (NICE) guidelines¹⁰ recommend a protein provision of 0.8 g/kg/BW/day and, specifically, advised not to offer a low protein diet of less than 0.6-0.8 g, also contradicting the 2020 KDOQI Guidelines.¹ The NICE guidelines¹⁰ are based on a low protein diet statement which was written in 2014 and, clearly, NICE felt that there was no new evidence, since 2014, to support a change in the guideline. In light of the conflicting evidence, it is the opinion of the author that protein requirements should be based using a patient-centred approach, assessing their nutritional status alongside their current protein intake, underlying diseases, CKD stage and its progression. While 0.8 g protein per kg/BW/day seems realistic to achieve for many people with kidney disease, some may benefit from a lower level.

“Low protein diets should not be used in patients with CKD who are malnourished/at risk of malnutrition, those who are unwell, admitted to hospital and in a catabolic state, as they represent a heterogeneous group, which differ from those with CKD who are metabolically stable.”

Protein requirements in people with CKD & hypercatabolism

When people with CKD, irrespective of their diabetes status, have an acute illness linked to a hospital admission or not, limiting protein intake to less than 0.8 g/kg/BW/day may no longer be appropriate (especially in the short-term). At present, the most recent guidelines on protein requirements in patients with CKD and hypermetabolism are from the European Society for Parenteral and Enteral Nutrition (ESPEN), published in 2021.²³ See **Table 2**.

These guidelines by Fiaccadori *et al.* state that protein provision should not be reduced to delay the initiation of dialysis in patient who are critically ill with CKD,²³ and this is a widely accepted expert opinion. In addition, Fiaccadori and colleagues suggest that patients should not follow a low protein regimen if the reason for their admission was an acute or associated to a hypermetabolic/catabolic event.²³ It is important to remember that the ESPEN guidelines²³ are based on the opinion of the authors only, and currently there is a significant lack of research on the optimal protein requirements in patients with CKD who are admitted to hospital.

It is the opinion of the author of this article that hospital diets should provide

a minimum of 0.8 g to 1 g protein/kg/BW/day, even in people with CKD admitted in hospital without critical illness. This is because, even in the absence of critical illness, people admitted to hospital are simply at higher risk of malnutrition. Furthermore, **Table 2** should not be interpreted that the maximum protein provision should be 1.3 g/kg/BW/day. Ultimately, patients with CKD admitted to hospital represent a heterogeneous group where conducting research is difficult. It is the patient-centred dietetic assessment (including nitrogen balance, anthropometry, marker of muscle function and muscle mass and kidney function), and the close monitoring of dietetic interventions, that should guide clinicians on what a patient's protein requirements are.

Conclusion

Guidelines are important documents to assist us in our practice, but it is important to understand how guidelines use the evidence to base their recommendations and their grading system.

In people with CKD and diabetes it seems appropriate to provide no more than 0.8 g/kg/BW/day.

Currently, NICE recommend a similar approach in people with CKD without diabetes (0.8 g/kg/BW/day) and Cochrane does not fully support the use of a low

protein diet in CKD without diabetes. On the other hand, KDOQI suggest a maximum intake of 0.6 g/kg/BW/day. It is the opinion of the author that until new RCTs (which should include updated medical treatments for patients with CKD as well data on quality of protein and QOL) are published, lowering protein intake to less than 0.8 g/kg/body weight should be exercised with caution (and in selected cases where the benefit outweighs the risk). In view of the conflicting evidence, using an individualised approach based on current eGFR progression, protein intake, and nutritional assessment, with the full involvement of patients within this decision-making process, seems the most sensible approach.

Low protein diets should not be used in patients with CKD who are malnourished/at risk of malnutrition, those who are unwell, admitted to hospital and in a catabolic state as they represent a heterogeneous group, which differ from those with CKD who are metabolically stable.

Protein requirements in CKD should be individualised using a patient-centred approach - utilising a dietetic assessment, full anthropometry, marker of muscle function, current protein intake, comorbidities, social and cultural preference and close monitoring.

Table 2: ESPEN protein guidelines recommendations for patients with CKD admitted to hospitals (not on dialysis)²³

	Protein requirements g protein/kg/BW/day	Level of evidence
CKD patients in hospital without critical illness	0.6-0.8 g	These are not based on RCT, systematic review or meta-analysis. Therefore, the level of evidence is confined to expert opinion only and should be interpreted with caution.
Patients with acute kidney injury (AKI) on CKD without an acute critical illness	0.8-1.0 g	
Patients with CKD or AKI on CKD with an acute critical illness	1.0-1.3 g	

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