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Elderly patients with chronic kidney disease: towards a better control of protein intake

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Editorial format

Title: Low protein diets for older patients: is consensus growing ?

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1 Recent data estimated that nearly 90% of individuals aged 65 years and older have at least
2 one chronic disease, with about 75% having two or more. Therefore, older adults represent a
3 growing proportion of patients with chronic kidney disease (CKD). The nutritional care of this specific
4 and expanding population is of significant importance, in order to avoid malnutrition or sarcopenia
5 and their related poor prognosis, as well as CKD progression to kidney failure. The recommended
6 daily protein intake for adults is 0.8 g/kg/day. However, the European Society for Clinical Nutrition
7 and Metabolism (ESPEN) recommends a higher daily protein intake of at least 1 g/kg and 30
8 kcal/kg/day, for older adults.¹ On the other hand, the 2020 Kidney Disease Outcomes Quality
9 Initiative (KDOQI) guidelines suggest a lower protein intake of 0.55-0.6 g/kg/day (or 0.28–0.43
10 g/kg/day with keto-acid analogs) for stable patients with non-dialysis CKD stages 3-5, and 0.6-0.8
11 g/kg/day for those with diabetes.² The energy intake should be within the range of 25-35
12 kcal/kg/day. It is important to note that ESPEN does not specifically address the case of CKD, and
13 KDOQI does not specifically focus on older individuals. These seemingly conflicting positions arise
14 from the limited knowledge of the actual protein needs of frail and ill older individuals, especially
15 those with CKD. Currently, scientific evidence, particularly from intervention trials, is insufficient to
16 provide concrete figures regarding protein requirements in this population. Thus, proposing
17 recommendations for protein intake in older adults with CKD poses a significant challenge.

18 Recently in *Clinical Nutrition*, ESPEN and ERN-ERA jointly published for the first time a critical
19 review paper regarding the optimal protein and energy intake for older adults with varying degrees
20 of CKD severity. These recommendations are based on expert opinions and are intended to aid
21 clinicians in designing personalized diets in older patients with non-dialysis CKD. Additionally, they
22 provide guidance on the effective implementation of these dietary approaches.³ This critical review
23 aims to address several significant questions: 1) What constitutes the definition of an older individual
24 with or without CKD ? 2) Which criteria can be used to define malnutrition? 3) Is there any evidence
25 supporting the effectiveness of low-protein diets (LPD) in older patients with CKD? Older adults
26 constitute a heterogeneous group, exhibiting a wide range of health conditions and functional status,
27 which are not reflected by chronological age. Thus, not all older adults with CKD require dietary
28 modifications with the implementation of a LPD. In fact, those with stable or slowly progressing CKD,
29 especially those at early stages of the disease, may not derive any benefits from an LPD, as they will
30 probably never reach kidney failure. Or at the opposite patients, patients with or at high risk of
31 malnutrition, with impairment in functional status or a limited life expectancy may also not benefit
32 from an LPD. This review provides a list of simple criteria to help clinicians choose between: “an
33 elderly and fragile patient with CKD” or “a patient with CKD who is also elderly”. (**Table 1**) The
34 authors also point out that management of this population is multidisciplinary, person-centered, with
35 a stepwise approach with initial evaluation and individualized assessment and monitoring. They

1 finally underline that the dietary advice must take into account many other factors (socio-economic,
2 eating habits, life expectancy, co-morbidity, dependency, cognitive status, etc.). Overall, this review
3 complements other nutritional recommendations that target specific populations, such as the
4 recently proposed guidelines for hospitalized patients with kidney disease.⁴

5 While this review has addressed several inquiries, numerous unresolved issues still remain.
6 Specifically, the potential benefits of LPD in terms of enhancing survival, quality of life and
7 nephroprotection for older adults have yet to be conclusively demonstrated through well-designed
8 and specific randomized controlled trials (RCT). Within the existing literature, large clinical trials that
9 contribute data to meta-analyses and guidelines often have limited recruitment of older and frail CKD
10 patients.⁵ There are only one RCT in selected older adults with eGFR (glomerular filtration rate) of 5
11 to 7 ml/min/1.73m² found that LPD permits to postpone dialysis start without increasing the risk of
12 death.⁶ This suggests that a LPD could be an effective treatment for conservative management of
13 CKD, which is often chosen by patients over 80 years old. However, other observational studies have
14 yielded conflicting results regarding the risk of kidney failure, and GFR decline associated with the
15 amount protein intake in older adults with CKD.⁷ In terms of survival, in the general population
16 without kidney disease, a LPD is associated with a reduction in mortality. However, this association
17 does not hold true for adults aged over 65 years.⁸ Similar observations have been found in patients
18 with CKD.⁹

19 Nevertheless, as highlighted in previous reviews on the same topic, pathophysiological
20 considerations support and make the reduction of protein intake in the presence of CKD very
21 attractive.¹⁰ LPD have been shown to reduce glomerular hyperfiltration, decrease the production of
22 uremic toxins, and mitigate acidosis, inflammation and metabolic complications, all of which are
23 factors involved in the progression of CKD. Are these nephroprotective mechanisms still applicable in
24 older adults with CKD? Indeed, the aging process and comorbidities commonly seen in the aged
25 population may influence the effectiveness of these mechanisms. There are arguments suggesting
26 that the kidneys' ability to compensate for increased protein intake by increasing GFR appears to be
27 preserved up to the age of 80.¹¹ This implies that a LPD may be theoretically effective in at least the
28 septuagenarians. Observational studies have found that adherence to a LPD in old men (aged 70–
29 71 years) with CKD stages 3-5 is associated with improved insulin sensitivity and decreased
30 inflammation.¹² Further specific studies in this population are required.

31 Another crucial aspect to consider is the high risk of malnutrition related to ageing and CKD.
32 Preliminary, defining malnutrition accurately is of utmost importance in order to closely monitor
33 these patients and identify individuals at risk of nutritional inadequacy. Major clinical nutrition
34 societies worldwide, under the Global Leadership Initiative on Malnutrition (GLIM), have

1 collaborated to establish a consensus definition for the diagnosis of malnutrition in adults.¹³ This
2 definition is independent of etiology and requires the presence of at least one phenotypic criterion
3 (such as non-volitional weight loss, low body mass index, or reduced muscle mass) and one
4 etiological criterion (such as reduced food intake or assimilation, and disease burden/inflammation).
5 No study has validated the application of these criteria specifically in patients with CKD who are over
6 70 years old. Furthermore, in the context of CKD, the term "protein-energy wasting" (PEW) is
7 preferred, and although the criteria used are similar, there are significant differences. The present
8 recommendations highlight the fact that standardizing the definition is desirable, as supported
9 elsewhere, but do not discuss in depth the available tools for nutritional assessment. PEW is a strong
10 predictor of mortality in patients with CKD, and it is also associated with sarcopenia, characterized by
11 a decline in muscle mass and strength.¹⁴ Protein intake plays a crucial role as an anabolic trigger for
12 muscle, promoting a positive muscle balance¹⁴ Both ageing and CKD are associated with an anabolic
13 resistance to proteins, resulting in a decrease in muscle protein synthesis. This phenomenon partly
14 explains the high prevalence of sarcopenia in older CKD adults, which is linked to falls, impaired
15 functional status, and increased mortality. While LPD has been found associated with muscle wasting
16 in non-dialysis CKD patients, the relationship between protein intake and muscle functional status
17 has been rarely studied in older patients with CKD. Recently, a short pilot RCT conducted in older
18 patients with CKD (mean age 81 years) showed that LPD had a favorable impact on nutritional
19 status.¹⁵ A long-term study and the utilization of muscle quality assessment tools are necessary to
20 ensure the safety of a LPD in older patients.

21 Further investigation is also needed about the role of protein type. Animal protein, in
22 comparison to plant-based protein, may pose greater risks to kidney health.¹⁶ There is some evidence
23 suggesting that the lower anabolic properties of plant-based foods may potentially impact muscle
24 mass and strength in older adults.¹⁷ Although no studies have specifically examined this issue
25 extensively in CKD patients, observational studies indicate that a diet rich in plant-based proteins is
26 associated with a reduced risk of developing new-onset CKD in middle-aged and older adults.¹⁸

27 In conclusion, for the first time, this critical review synthesizes the existing body of
28 knowledge on the impact of dietetics on nephroprotection in older adults, focusing on the specific
29 challenges faced. They conclude that a one-size-fits-all approach may be inappropriate in this
30 population, and they explain that it is not possible to propose a single threshold for protein intake. It
31 emphasizes the importance of offering nephroprotective diets only to a specific population of older
32 individuals.³ While there are still many aspects that require further in-depth investigation, this review
33 provides a starting point for collective reflection. It presents an opportunity for future studies to
34 address these remaining questions and contribute to our understanding of the topic. Without such

1 studies, it will be difficult to convincingly advocate for the usefulness of LPD regimens, and to
2 overcome the barriers associated with their implementation in older adults for whom they might be
3 beneficial.

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2 **Table 1 : Criteria to help clinicians prioritize protein intake in older patients**

NUTRITIONAL PRIORITY (high protein diet)	RENAL PRIORITY (low protein diet)
Diagnosis of malnutrition-PEW	Advanced CKD (e.g. Stage 4–5)
Early CKD stage (e.g. Stage 3a-3b)	Rapid CKD progression
No or slow CKD progression	Uremic symptoms
Comorbidities and short life expectancy	Good nutritional status

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4 **Abbreviation:** CKD: Chronic Kidney Disease; PEW : Protein-Energy Wasting

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