

The Real Clinical Utility of Low-Protein and Protein-Free Foods in Chronic Kidney Disease: A Forty-Year Perspective

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Abstract

Over the past forty years, Low-Protein Diets (LPD) and Very-Low-Protein Diets (VLPD) supported by protein-free foods have shaped conservative CKD management, especially in Italy. These foods-mainly protein-free bread, pasta and flour substitutes-allow patients to maintain adequate caloric intake while reducing nitrogenous waste, phosphorus load and metabolic acidosis. Although randomized trials isolating their specific contribution are lacking, observational evidence consistently shows that LPD/VLPD supported by protein-free foods can delay dialysis, improve metabolic parameters and preserve nutritional status in selected patients. This review revisits four decades of clinical experience, from the pre-RAASi era to the modern landscape shaped by SGLT2 inhibitors and Finerenone.

Keywords: Chronic Kidney Disease; Low-Protein Diet; Very-Low-Protein Diet; Protein-Free Foods; Renal Survival; Metabolic Control; Nutritional Status; Conservative Management; Dialysis Postponement; Italy; Forty-Year Experience

Introduction

The concept of dietary protein restriction in CKD dates back to the 1960s and Italy soon became a leading center for structured LPD and VLPD programs. As protein restriction intensified -0.6 g/kg/day for LPD and 0.3-0.4 g/kg/day for VLPD-clinicians needed a way to maintain adequate caloric intake without increasing nitrogen load. Protein-free foods were developed precisely for this purpose, enabling patients to reach 30-35 kcal/kg/day while adhering to strict protein limits [1-3]. The MDRD study later questioned the impact of protein restriction on GFR decline but long-term Italian cohorts told a different story,

showing delayed dialysis, improved metabolic control and preserved nutritional status in adherent patients [4].

Materials and Methods

This narrative review integrates historical Italian cohorts from the 1980s to the 2020s, observational studies on renal survival and metabolic outcomes and controlled trials involving VLPD with ketoanalogues, where protein-free foods were essential for adherence. Because no study isolates protein-free foods as a single variable, their utility is inferred from the broader dietary regimens in which they play a central enabling role [1-9].

Results

1. Impact on Progression to Kidney Failure

Across multiple Italian cohorts, patients adhering to LPD/VLPD supported by protein-free foods consistently delayed dialysis initiation. Reported delays range from 12 to 24 months compared with unrestricted diets [5-7]. Long-term observational studies show a 30-60% reduction in the risk of ESKD [6,8]. These benefits are most evident in younger, motivated patients with stable nutritional status.

2. *Metabolic Benefits*

Protein-free foods contribute to several clinically meaningful metabolic improvements:

Lower serum urea and improved uremic symptoms [1,5].

Reduced phosphorus intake and better phosphate control [2,6].

Improved correction of metabolic acidosis, especially with bicarbonate supplementation [3].

Lower sodium intake compared with standard cereal products [2].

These effects reflect the broader metabolic advantages of protein restriction, but protein-free foods make such restriction sustainable.

3. *Nutritional Status*

When caloric intake is maintained above 30 kcal/kg/day, nutritional status remains stable. BMI, serum albumin and body composition were preserved in most cohorts [5,7,9]. Malnutrition occurred primarily when caloric intake dropped below 25-30 kcal/kg/day, not because of protein-free foods themselves [9].

4. *Adherence and Feasibility*

Protein-free foods improve adherence by allowing patients to maintain familiar dietary patterns-pasta, bread, baked goods-despite strict protein restriction. However, long-term adherence varies widely (30-70%), influenced by taste, cost and regional availability [6,9].

5. *Role in the Modern Therapeutic Era*

With the advent of RAAS blockade, SGLT2 inhibitors and finerenone, the relative weight of dietary therapy has decreased. Yet the absolute utility of protein-free foods remains significant for patients aiming to postpone dialysis, those with contraindications to aggressive pharmacologic therapy and motivated individuals with good nutritional reserve [6-8].

Discussion

The assessment of the real usefulness of protein-free foods in the course of Chronic Kidney Disease (CKD) represents a topic that has accompanied more than forty years of nephrological practice, evolving in parallel with the epidemiological, therapeutic and cultural changes of renal disease. Historical and contemporary literature shows that these products have never been merely “substitute foods,” but therapeutic tools integrated into a broader dietary paradigm aimed at reducing nitrogenous waste, controlling calcium-phosphate metabolism and modulating CKD progression [1-4].

A first key element is that the introduction of protein-free foods made low-protein diets truly feasible as early as the 1970s and 1980s, overcoming the limitations of monotony, poor palatability and the risk of malnutrition that characterized severe protein restriction. The Italian experience-unique worldwide for its breadth, continuity and depth-has demonstrated that dietary adherence increases significantly when patients have access to substitutes for bread, pasta, flour and baked goods that preserve culturally rooted eating habits [5-7]. This aspect, often underestimated, has a direct impact on quality of life and on the long-term sustainability of conservative treatment.

At the same time, clinical evidence has progressively clarified that protein restriction, when properly balanced and supported by protein-free foods, reduces the production of urea, phosphate and uremic toxins derived from protein metabolism, with favorable effects on symptom control and CKD progression [8-11]. Italian observational studies involving thousands of patients have documented a slower decline in glomerular filtration rate and a significant delay in dialysis initiation, with both clinical and economic benefits for the healthcare system [12-14].

A crucial point concerns nutritional safety. Historical criticisms of low-protein diets-risk of protein-energy wasting, loss of muscle mass, deterioration of functional status-have been progressively mitigated by studies showing that such risks emerge almost exclusively in the absence of adequate caloric intake and without the use of energy-dense protein-free foods [15-17]. When the diet is well structured, personalized and monitored, the nutritional profile remains stable and, in many cases, improves thanks to the reduction of metabolic inflammation and chronic acidosis.

Another relevant aspect is the role of protein-free foods in the modern era, characterized by an older CKD population, complex comorbidities and widespread use of nephroprotective drugs such as SGLT2 inhibitors and RAAS blockers. Clinical experience from the last decade suggests that low-protein diets supported by protein-free foods have not lost relevance; rather, they integrate with pharmacological therapies, contributing to a multimodal nephroprotective strategy [18-20]. In particular, among frail elderly patients, the ability to modulate protein intake without compromising caloric supply represents a strategic advantage.

Finally, the social and cultural dimension should not be overlooked. In Italy, the availability of protein-free foods through the National Health Service has represented a model of therapeutic equity recognized internationally. Free or reimbursed access has prevented economic disparities and ensured continuity of care even for the most vulnerable segments of the population, contributing to better and more homogeneous clinical outcomes [21,22].

Overall, the discussion emerging from the last forty years shows that protein-free foods are not a simple dietary complement but a structural component of conservative CKD therapy. Their usefulness emerges not only on metabolic grounds but also on nutritional, psychological, social and organizational levels. Their effectiveness depends on the nephrologist's ability to integrate them into a personalized, monitored and culturally sustainable care pathway, confirming the central role of diet therapy in the modern management of chronic kidney disease.

Conclusion

Across forty years of clinical practice, protein-free foods have proven to be essential enablers of effective protein restriction. By supporting adequate caloric intake, improving metabolic control and contributing to delayed dialysis initiation, they remain a valuable option for selected CKD patients. Their role has evolved but remains meaningful within a multimodal nephroprotective strategy.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

Ethical Statement

The project did not meet the definition of human subject research under the preview of the IRB according to federal regulations and therefore was exempt.

Informed Consent Statement

Informed consent was obtained from all participants included in the study.

Authors' Contributions

All authors contributed equally to this paper.

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