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Going Nuts to Protect Kidneys and to Live Longer with Kidney Disease

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Nuts have been prominently highlighted across multiple dietary recommendations and guidelines as nutrient-dense foods that are rich in minerals, vitamins, unsaturated fatty acids, and fiber. According to the US Department of Agriculture's Economic Research "Service Food Availability (Per Capita) Data System" (FADS), the annual consumption of nuts in the USA has grown from 1.38 pounds per person in 1970 to 3.69 pounds per person in 2016. In the general population, epidemiologic studies have shown that higher nut consumption is associated with better health outcomes, including lower risk of cancer, obesity, and all-cause and cardiovascular disease (CVD)-related mortality [1, 2].

The health benefits of nuts have been well described and exhibit biologic plausibility given their nutrient composition. First, nuts are rich in dietary potassium, which is the key electrolyte needed for critical cell functions including muscle contraction and cardiac conduction. Prescribed-diets that are rich in potassium from nuts, such as the "Dietary Approaches to Stop Hypertension" (DASH) diet, have been shown to attenuate CVD risk [3]. Seconds, nuts are a key source of micronutrients (antioxidants) and dietary fiber, the latter of which is needed to process/absorb nutrients and has demonstrated salutary benefits, including improved blood pressure, glycemic control, dyslipidemia, gastrointestinal motility/constipation, and gut microbiota composition [4]. Third, in heathy *Food Exchange* lists, which group together foods with similar qualities providing the same nutritional value when exchanged for one another, nuts are oftentimes included as a dietary fat source given their high mono- and poly-unsaturated fatty acid and lower saturated fat content, characterized by more plant omega-3 including alpha-linolenic acid. Compared with legumes as another main food consumed in plant-based diet plans, nuts tend to have even greater vegetable oils, less carbohydrates, and roughly similar amounts of plant-based protein per serving. Both nuts and legumes are packed with antioxidant vitamins and essential minerals and have favorable plant-based protein profiles in order to optimize health. Other advantageous features of nuts compared to legumes include their convenience as a healthy "snack," given that nuts typically do not require cooking, have longer preservation at room temperature, and are light/compact and easily portable (Table 1).

The high mineral content of nuts has traditionally led to likely unsubstantiated recommendations to avoid nuts in chronic kidney disease (CKD). Nuts have high phosphorus content, which is one of the common nutrients restricted in advanced CKD to avoid perceived risk of hyperphosphatemia. However, dietary phosphorus has varying absorbability based on its type (organic vs. inor-

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Table 1. Nutrient composition of nuts per one serving (28 g/1 oz) of raw nuts

Nuts	Nutrient															
	energy, kcal	macronutrients, g						fiber, gmineral, mg						Phytochemical (antioxidant), mg		Vitamin, mg
		protein	fat	fatty acids			carbo-hydrate		Ca	Mg	K	P	Na	Phytosterols[a]	Total phenols	Vitamin E (α-tocopherol)
			total	SFA	MUFA	PUFA										
Almond	162	5.9	14.0	1.1	8.8	3.4	6.0	3.5	75	76	205	135	0	55.2	80	7.2
Brazil nuts[b]	185	4.0	18.8	4.5	6.7	6.8	3.3	2.1	45	105	185	203	1	34.6	68	1.6
Cashews	155	5.1	12.3	2.2	6.7	2.2	8.5	0.9	10	82	185	166	3	42.3	38	0.3
Hazelnuts	176	4.2	17.0	1.3	12.8	2.2	4.7	2.7	32	46	190	81	0	34.2	192	4.2
Macadamias	201	2.2	21.2	3.4	16.5	0.4	3.9	2.4	24	36	103	53	1	32.5	35	0.1
Peanuts	159	7.2	13.8	1.8	6.8	4.4	4.5	2.4	26	47	197	105	5	NA	114	2.3
Peacans	193	2.6	20.2	1.7	11.4	6.0	3.9	2.7	20	34	115	78	0	44.5	360	0.4
Pine nuts[b]	188	3.8	19.2	1.4	5.3	9.5	3.7	1.0	4	70	167	161	1	66.1	9	2.6
Pistachios	157	5.7	12.7	1.7	6.5	4.0	7.6	3.0	29	34	287	137	0	59.9	243	0.8
Walnuts[c]	183	4.3	18.3	1.7	2.5	13.2	3.8	1.9	27	44	123	97	1	30.9	441	0.2
Recommended Daily intake In advanced CKD	30–35/kg	0.6–0.8/kg	Mostly MUFA and PUFA, including *n*-3 fatty acids					>30	800–1,000		<3,000[d]	<800	<3[e]			

Nutrient information is taken from the United States Department of Agriculture (USDA) Nutrient Database Standard Reference, Release 28. MUFA, monounsaturated fatty acids; NA, not available; PUFA, polyunsaturated fatty acids; SFA, saturated fatty acids. [a]Phytosterols are the sum of stigmasterol, campesterol, β-sitosterol, and other phytosterols. [b]Dry roasted. [c]English variety. [d]If hyperkalemia occurs frequently during high-fiber intake. [e]Avoid intake of <1.5 if hyponatremia likely.

ganic) and source (animal vs. plant). Given that nuts contain organic phosphorus and are considered a plant-based phosphorus source, which typically occur in the form of phytates and have much lower bioavailability due to lack of the degrading enzyme phytase in humans, it is highly unlikely that they contribute to dietary phosphorus burden in CKD [5]. Furthermore, nuts are usually not cooked, and hence, it is highly unlikely that they contribute to dietary phosphorus burden in CKD (<30% absorbed, particularly if uncooked). The high potassium content of nuts and potential risk of hyperkalemia may be another concern among CKD patients. However, growing evidence has suggested that lower dietary potassium intake is associated with worse survival in both non-dialysis dependent and dialysis-dependent CKD patients [6, 7]. Another unfounded concern relates to the high magnesium content of nuts, considering that epidemiologic studies have consistently confirmed the benefits of high dietary magnesium intake. While nuts are considered a healthy food in the general population, there has been a paucity of research examining the impact of nut consumption upon outcomes in patients with CKD.

In this issue of *AJN*, Wang et al. [1] present data examining the association between frequency of nut consumption ascertained by Food Frequency Questionnaires (FFQs) with the prevalence of CKD as well as the risk of all-cause and CVD mortality among 6,072 adults, comprised of 1,203 participants with CKD and 4,869 participants without CKD, from the US National Health and Nutrition Examination Study (NHANES) cohort surveyed over 2003–2006. Frequency of nut consumption in the preceding 12 months was categorized as (1) never, (2) 1–11 times per year, (3) 1–3 times per month, (4) 1–6 times per week, and (5) more than once a day, with those who have never consumed nuts as the reference group. Consuming nuts 1–6 times per week (i.e., second highest category of nut consumption frequency) was associated with a 33% lower prevalence of CKD in analyses that accounted for key confounders such as socio-demographics, dietary intake (energy, protein, fat, carbohydrate, sugar), lifestyle factors (smoking, alcohol use), presence of selected chronic conditions (obesity, hypertension, diabetes), and serum lipid levels. Higher nut consumption was significantly associated with lower all-cause and CVD mortality in non-CKD participants. Among CKD participants, across the various exposure groups, those who consumed nuts 1–6 times per week exhibited a 37% lower risk of all-cause mortality after adjusting for potential cofounders including those in the abovementioned CKD analyses, as well as additional laboratory covariates (eGFR, UACR, serum potassium, serum phosphorus), comorbidities (coronary heart disease, congestive heart failure, stroke, cancer), and dietary factors (fatty acids, phosphorus, sodium, potassium consumption). While point estimates suggested that greater nut consumption of 1–6 times per week was associated with lower CVD mortality risk among those with CKD in fully adjusted analyses, associations did not quite reach statistical significance.

The study by Wang et al. [1] adds important knowledge to the field by demonstrating the favorable impact of nut intake on CKD progression as well as all-cause and CVD mortality risk, irrespective of underlying CKD status. Although there were consistently incremental trends between higher frequency of nut consumption and lower all-cause and CVD mortality in participants without CKD, this pattern of associations was not observed in those with CKD (i.e., non-dose dependent relationship between nut intake and mortality in CKD), emphasizing the importance of eating an appropriate amount of nuts once CKD has developed. With respect to practical and safe implementation, nuts may be incorporated into a patient-centered diet comprised of the plant-dominant low-protein or PLADO diet consisting of dietary protein intake of 0.6–0.8 g/kg/day with ≥50% from plant-based sources, which has been recommended in the nutritional management of NDD-CKD [8].

Several limitations should be considered when interpreting the study's findings. First, as this was a cross-sectional study that only assessed baseline nut consumption, the causality effect of nut intake on CKD and mortality outcomes, as well as the longitudinal impact of varying nut consumption over time upon these endpoints remains unclear. It is also possible that more frequent ingestion of nuts is a surrogate of a healthier diet/lifestyle, notwithstanding the multivariate adjustment for potential dietary/lifestyle confounders in this study. Finally, given that (1) FFQs have a tendency toward non-differential underestimation of nutrient intake in comparison to real-time dietary assessments and that (2) serving size was not ascertained by these FFQs, precise agreement between the actual versus reported amount and frequency of nut consumption is unclear.

It also bears to mention that there are remaining knowledge gaps of the effects of different types of nut intake among NDD-CKD and dialysis-dependent CKD patients, rendering compelling need for future research in this area. Given the growing global CKD population and ongoing debate as to whether nut consumption is beneficial for CKD patients in light of their heart-healthy-nu-

trient content as well as dietary elements that are typically avoided in advanced kidney disease, the study by Wang et al. [1] is an important contribution to the field by underscoring nut consumption as a salutary food in the CKD diet. These data also highlight that portion size is a key consideration and that future research defining the optimal intake of nut consumption in CKD patients are needed.

Conflict of Interest Statement

C.M.R. has received honoraria from AstraZeneca, Ardelyx, Dexcom, Fresenius, Otsuka, Reata, and Recor. None of the other authors have relevant disclosures to report.

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Author Contributions

Y.N., C.M.R., and K.K.-Z. wrote the manuscript; K.K.-Z. had primary responsibility for final content. All authors read and approved the final manuscript.

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