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In Focus

DASH-ing toward improved renal outcomes: when healthy nutrition prevents incident chronic kidney disease

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Chronic kidney disease (CKD) affects a substantial proportion of the general population worldwide [1]. The burden of CKD on affected individuals and on the society are now well-documented [2], emphasizing the need for better preventive efforts. Treatment of well-known risk factors such as hypertension or diabetes mellitus can be applied to this end, but interventions that could be applied to the wider general population (e.g. life style modification) are less well defined. Healthy nutrition can indeed be envisioned as such an 'intervention', in that diets consisting of proper amounts and quality of nutrients could have potentially far reaching positive consequences. One such dietary intervention, the DASH (Dietary Approaches to Stop Hypertension) diet, has been particularly well studied. The DASH diet is rich in fruits, vegetables, low-fat dairy products, potassium, calcium, magnesium and fibers, while it is low in saturated fat, sodium, added sweeteners and other sugars and additives such as inorganic phosphorus (Table 1). The macronutrient breakdown of the classical DASH diet is approximately 55% carbohydrates, 18% protein and 27% fat as the source of energy, but there are different DASH versions [3]. The DASH emphasizes healthy sources of protein, such as, lean meats, nuts, seeds, and legumes as well as complex carbohydrates such as whole grains. The original purpose of the DASH diet was to lower blood pressure in patients with prehypertension or stage I hypertension [4]. Subsequent secondary analyses and observational studies have suggested that consumption of the DASH diet is also associated with lower incidence of coronary heart disease and stroke [5, 6]. The association of the DASH diet with CKD has also been examined in selected Western populations, suggesting a potential protective effect [7, 8].

One potential problem inherent of even the best-designed clinical trials is their limited external validity; i.e. their results apply primarily to patients whose characteristics are similar to those of the original trial participants [9]. This issue is particularly compelling when we try to extrapolate a dietary intervention to populations from countries with a vastly different socio-cultural milieu, as their dietary habits and the available nutrients could be fundamentally different. It is thus very important that interventions examined in Western populations are tested in other countries to determine the degree to which they could confer similar benefits.

Such a confirmatory study was conducted by Asghari *et al.* and is published in this issue of *Nephrology Dialysis Transplantation* [10]. The investigators used a prospective health survey conducted in Tehran (the Tehran Lipid and Glucose Study) to select randomly a group of 3462 participants for a dietary assessment, of which 1630 individuals were included in the present analysis. Participants completed a detailed, validated food frequency questionnaire, which was used to determine their adherence to a DASH-style diet, and to quantify the various components of their diet. Participants were followed for a median of 6.1 years, and the outcome of interest was incident CKD, defined as the occurrence of an estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2. Adherence to a DASH-style diet was associated with a 60% lower incidence of CKD after adjustment for a battery of confounders. When examining individual components of the DASH diet, higher consumption of fruits, whole grains, nuts and legumes was also associated with lower incidence of CKD [10].

The health benefits of a DASH-style diet are potentially far-reaching, although the mechanisms whereby a DASH diet

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Table 1. Daily and weekly DASH eating plan goals for a 2000-calorie-a-day diet (adapted from the National Heart Lung, and Blood Institute of the National Institutes of Health, https://www.nhlbi.nih.gov/health/health-topics/topics/dash)[a]

Food group	Daily servings
Grains	6–8
Meats, poultry and fish	6 or less
Vegetables	4–5
Fruit	4–5
Low-fat or fat-free dairy products	2–3
Fats and oils	2–3
Sodium	2300 mg[b]
	Weekly servings
Nuts, seeds, dry beans and peas	4–5
Sweets	5 or less

[a]Note that the DASH is a flexible and balanced eating plan that helps create a heart-healthy eating style for life. The DASH eating plan requires no special foods and instead provides daily and weekly nutritional goals. This plan recommends: eating vegetables, fruits and whole grains; including fat-free or low-fat dairy products, fish, poultry, beans, nuts and vegetable oils; limiting foods that are high in saturated fat, such as fatty meats, full-fat dairy products, and tropical oils such as coconut, palm kernel and palm oils; limiting sugar-sweetened beverages and sweets.
[b]1500 milligrams (mg) sodium lowers blood pressure even further than 2300 mg sodium daily.

could impact health outcomes, and specifically the incidence of CKD, remain speculative. Changes introduced by a complex dietary intervention could affect both the quantity and the quality of nutrients in a way that affects multiple pathophysiologic processes. The most conspicuous positive benefits of a DASH diet would be its effects on blood pressure lowering [11], and also its beneficial effects on the lipid profile [12]; both of these could serve as putative reasons for improved renal outcomes. Further renal benefits could be conferred by a higher dietary potassium content in the DASH diet [13], the lower amount [14, 15] and the different quality (plant, as opposed to animal-based) of dietary protein [16], a lower acid load [17], and potential anti-inflammatory and antioxidant effects from plant-based micronutrients and high fibers that may favorably modulate the microbiome [18].

Somewhat surprising and seemingly counterintuitive were findings in the study by Asghari *et al.* that higher consumption of sweetened beverages and sodium were also associated with lower CKD incidence [10]. Other studies that examined the association of urinary sodium with progression of CKD showed inconsistent findings [19, 20]. These inconsistencies may reflect the heterogeneity of the studied populations (which included patients enrolled in various clinical trials, and also patients enrolled in prospective cohorts), but also the fact that single collections of urine sodium may not accurately reflect dietary sodium intake [21]. The use of a food frequency questionnaire by Asghari *et al.* would therefore constitute a definitive advantage, notwithstanding some inherent limitations of these questionnaires such as suboptimal precision at individual level although adequate for comparative nutritional studies at population level. A possible explanation for the association of higher sodium consumption with a lower incidence of CKD could be that the definition of incident CKD used by Asghari *et al.* used a single eGFR <60 mL/min/1.73 m2, which could have included episodes of transient declines in kidney function (acute kidney injury), which could have occurred more frequently among individuals with lower sodium intake due to a predisposition to hypovolemia. Furthermore, volume depletion has also been implicated as a potential cause of certain nephropathies such as Mesoamerican nephropathy [22], suggesting that higher sodium intake may indeed confer long-term renal benefits among individuals living in hot climates.

Major advantages of the study include the use of a complex validated 168-question food frequency questionnaire, and a prospective cohort design with high-quality data and low loss of follow-up. Limitations of the study include the lack of a complex survey strategy (which could have made the results more representative of the wider Iranian population) and the use of a CKD definition that did not include a repeat eGFR measurement, new onset proteinuria or a certain minimum threshold for the decrease in kidney function. These limitations in the definition of CKD could have resulted in false-positive CKD cases as a result of acute kidney injury or merely due to a slight decrease in kidney function as a result of ageing. The latter concern is somewhat alleviated by the fact that the results were unchanged in a sensitivity analysis that used a 25% decrease in eGFR as an additional prerequisite of the CKD diagnosis.

The study by Asghari *et al.* offers important insight into the benefits of the nutritional management for prevention of chronic diseases in general and the favorable effects of DASH diet in a population that is distinctly different from the original DASH trial population, in this case a thriving Middle-Eastern society with an emerging economy that is increasingly subject to unhealthy nutrition as it continues to adopt a westernized life style. There could be important differences in how patients of different race respond to the DASH diet, as indicated by the greater efficacy on clinical end points in African American participants of the DASH trial [23]. Notwithstanding the lack of a clear explanation, the fact that the benefits of the DASH diet are apparent in an Iranian population offers important additional evidence for the wider external validity of a dietary approach to mitigate progressive loss of kidney function.

The totality of the evidence indicates that the benefits of a healthy diet such as the DASH diet could be far-reaching, and a population-wide promotion of such diets may offer substantial benefits. It behooves the policymakers of various countries to recognize the long-term benefits of healthy diets, and to implement regulations that make such interventions possible. Such far-reaching interventions require visionary action and large scale investment. One can only hope that studies such as the one by Asghari *et al.* will help convince the public and politicians alike about the worthwhile nature of such investment.

CONFLICT OF INTEREST STATEMENT

C.P.K. has received honoraria from Astra-Zeneca, Relypsa, Sanofi-Aventis and ZS Pharma. K.K.-Z. has received honoraria from Abbott, Abbvie, Alexion, Amgen, Astra-Zeneca, Aveo, Chugai, DaVita, Fresenius, Genentech, Haymarket Media, Hospira, Kabi, Keryx, Novartis, Pfizer, Relypsa, Resverlogix, Sandoz, Sanofi, Shire, Vifor, UpToDate and ZS-Pharma.

(See related article by Asghari *et al.* The association between Dietary Approches to Stop Hypertension and incidence of chronic kidney disease in adults: the Tehran Lipid and Glucose Study. *Nephrol Dial Transplant* 2017; 32 (Suppl 2): ii224–ii230)

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