

A Narrative Review of Dietary Approaches for Kidney Transplant Patients



Laura Goldfarb Cyrino^{1,2}, Jennie Galpern¹, Lori Moore³, Lea Borgi³ and Leonardo V. Riella^{1,2}

¹Center for Transplantation Sciences, Department of Surgery, Massachusetts General Hospital, Boston, Massachusetts, USA; ²Division of Nephrology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts, USA; and ³Division of Nephrology, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts, USA

A healthy eating pattern has proven to lower the risk of metabolic and cardiovascular diseases. However, there are sparse dietary recommendations for kidney transplant recipients, and the ones available focus only on single nutrients intake, such as sodium, potassium, and proteins, and not on the overall eating pattern. Considering that individuals do not typically consume nutrients in isolation, but as part of a complete dietary pattern, it is challenging for the average transplanted patient to understand and implement specific dietary recommendations. Also, single-nutrient interventions demonstrate largely inconclusive effects, and it seems improbable that they could have a strong enough impact on transplant outcomes. Dietary trends such as plant-based diets, intermittent fasting, low-carb diet/keto-diet, and juicing, have gained major attention from the media. Herein, we review the potential risks and benefits of these diets in kidney transplant recipients and provide an updated dietary recommendation for this population with consideration of current nutritional trends. Overall, the Mediterranean and DASH diets have demonstrated to be the most beneficial dietary patterns to the post kidney transplant population by focusing on less meat and processed foods, while increasing the intake of fresh foods and plant-based choices. We believe that to maintain a healthy lifestyle posttransplant, patients should be educated about the scientific evidence of different diets and choose a dietary pattern that is sustainable long-term.

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kidney disease affects 1 in every 10 individuals, and kidney transplantation is the best treatment option for patients with advanced kidney disease. Despite many advances since the first kidney transplant in 1954, little progress in the improvement of long-term graft survival has been achieved. While many immunological and donor-related factors may affect the expected life of a kidney transplant, the diet and lifestyle of transplant recipients are clear drivers of comorbidities, including cardiovascular disease and diabetes. With that in mind and faced by many different media trends in diet recommendations for the general population, updated dietary information specifically for kidney transplant recipients is crucial.

Current evidence-based guidelines recommend dietary interventions for kidney transplant recipients

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that target single nutrients, such as sodium, protein, phosphorus, and potassium. However, individuals do not typically consume these nutrients in isolation, but as part of a complete dietary pattern. Therefore, it is challenging for the average patient to understand and implement specific dietary recommendations, particularly when multiple restrictions are prescribed simultaneously, an individualized approach is not used, and emphasis is placed on what foods to avoid rather than what foods to consume. In addition, single-nutrient interventions have demonstrated largely inconclusive effects, and it seems improbable that a single nutrient or food could have a strong enough impact to substantially change graft failure rates. However, dietary patterns as a whole, such as plant-based diets, have been associated with improved outcomes for patients with kidney disease, and general healthy eating (consumption of variety of unprocessed foods that helps maintain or improve overall health) is also protective against many chronic diseases, including diabetes, obesity, and cardiovascular disease.

Correspondence: Leonardo V. Riella, Massachusetts General Hospital, Harvard Medical School, 55 Fruit Street, Boston, Massachusetts 02115, USA. E-mail: Iriella@mgh.harvard.edu

Modifying dietary patterns as a whole may present an alternative or complementary approach to singlenutrient interventions. An emphasis on translating dietary recommendations into clinical practice is a lowcost strategy expected to improve patient understanding and, ultimately, compliance, carrying potential benefits beyond the health of the kidney, but for the overall health of the transplant recipient. Lifestyle interventions, such as increase in exercise and healthy dietary changes, can have an impact greater than any individual medication with significantly lower cost. Thus, this review seeks to discuss different dietary patterns and their possible effects on kidney transplant recipients.

Dietary Trends and Their Impact in Kidney Transplant Recipients

In the past 10 years, several dietary trends emerged claiming reduction in cardiovascular risk, antiinflammatory effects, and weight loss. Among those, plant-based diets, intermittent fasting, low-carb diet/ keto-diet, and juicing have gained major attention from the media. We, therefore, describe the potential risks and benefits of these diets in kidney transplant recipients.

Plant-Based Diets

Plant-based diets are becoming increasingly popular. Doctors have certainly recognized the potential impact of following a plant-based diet on overall health. In the Adventist Health study, a plant-based diet approach reduced all-cause mortality (hazard ratio 0.88; 95% confidence interval 0.80-0.97).¹ A plant-based dietary pattern is primarily composed of whole grains, fruits, vegetables, legumes, nuts, and seeds. Animal foods, such as meat, poultry, fish, eggs, and dairy are consumed in small amounts or excluded entirely, making these diets lower in animal protein than a typical Western diet.² The many different types of plant-based diets should be considered on a spectrum, with vegetarian and vegan diets being the most restrictive, as they exclude meat-based foods entirely.

Evidence supports the positive effects of plant-based dietary patterns when compared with the meat-based Western diets with regard to kidney function.^{3–5} High intake of meat is positively associated with albuminuria,⁶ and production of nitrogen products requiring elimination by the kidneys. In contrast, consumption of fruits and vegetables is inversely associated with albuminuria.^{6,7} In 3972 patients with chronic kidney disease (CKD), a graded association between higher unhealthy diet pattern scores and a higher risk of all-cause mortality was demonstrated. In contrast, the high consumption of a diet rich in fish,

fruits, and vegetables was associated with a lower mortality risk over time.⁸ Plant-based diets in individuals with an estimated glomerular filtration rate (eGFR) of 30 to 59 ml/min may delay progression to end-stage kidney disease (ESKD) and potentially improve survival.⁴ In 14,686 adults followed for 24 years, higher adherence to a healthy plant-based diet was associated with a 14% reduction in the risk of CKD, and slower eGFR decline, whereas lower adherence was associated with an 11% higher risk of CKD.⁹

In the following, we review and evaluate the risks and benefits of the most plant-based dietary trends in post kidney transplant patients: Mediterranean, Dietary Approaches to Stop Hypertension (DASH), and vegetarian/vegan diets.

Mediterranean Diet. A Mediterranean diet is traditionally from the Mediterranean Sea's shores. It is based on a high intake of virgin olive oil, vegetables, fruits, whole grains, fish, low-fat dairy, moderate alcohol intake (wine), and low red meat consumption (Supplementary Table S1).¹⁰ Evidence suggests that adherence to this diet reduces the risk of diabetes, cardiovascular disease, and mortality.¹¹ Specifically, this diet has shown benefits in reducing inflammation, oxidative stress, endothelial dysfunction, acidosis, hyperlipidemia, hyperglycemia, and blood pressure (BP) levels.4,9,12-14 Studies not only in the general population but also in kidney transplant recipients associate a Mediterranean Diet Score with favorable clinical endpoints including kidney function.^{12,15} In a multiethnic cohort of 3298 individuals with 15-year follow-up, a score at or above the median was associated with an approximate 50% decreased odds of developing incident eGFR <60 ml/min per 1.73 m².¹⁵ Moreover, in 632 transplant recipients, an inverse association with all study endpoints (graft failure, kidney function decline, and graft loss) and adherence to the diet was demonstrated, especially in those with more proteinuria.¹²

This diet is also able to reduce oxidative stress, inflammation, and atherosclerosis because of a high intake of unsaturated fat (olive oil) and polyphenols (red wine),^{16,17} and low saturated fat intake (red meat).^{18,19} In transplant recipients, this diet showed improvement on oxidative status of the plasma and erythrocytes¹⁶ and also on acid-base balance and glomerular hemodynamics.^{3–5,12–16} Thus, we strongly recommend this diet, as it leads to a balanced eating habit with a positive impact on overall health and graft survival after transplantation.

DASH Diet. Designed by the National Institutes of Health to treat or prevent high BP, this diet consists of a

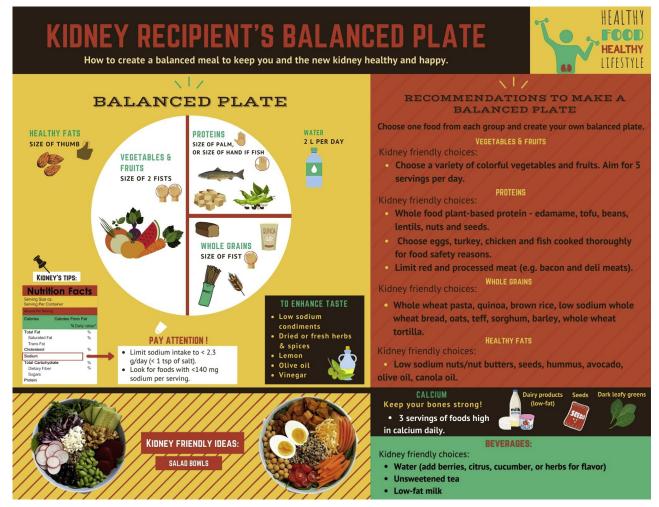


Figure 1. Kidney recipient's balanced plate. Illustration depicting recommendations and balanced plate visuals for kidney transplant recipients.

low intake of sodium and red/processed meat, moderate intake of fish, poultry, nuts, and seeds, and high intake of vegetables, fruits, whole grains, and low-fat dairy products. This diet is also high in fiber and monounsaturated fats, and low in saturated, trans, and total fat.

Americans consume more than 3400 milligrams per day of sodium,²⁰ which exceeds the average of 2300 milligrams recommended by the 2015–2020 Dietary Guideline.^{21,22} A high-salt diet is associated with a number of complications, including hypertension and cardiovascular events. Moreover, our group has previously shown that sodium promotes acute rejection in mice.²³ The DASH diet significantly improves BP, total cholesterol, and low-density lipoprotein concentrations.²⁴ In an 8-week controlled feeding clinical trial in a cohort with or without hypertension, the DASH diet had a greater potential to lower BP (by 5.5 and 3.0 mm Hg for systolic and diastolic BP, respectively) when compared with a regular diet, or a diet rich in fruits and vegetables.²⁵

The DASH diet continues to be considered as the most efficient diet to control hypertension,²⁶ which is

common in kidney transplant recipients. Hypertension affects 50% to 80% of adult transplant recipients²⁷ and contributes to shortened allograft survival and increased cardiovascular morbidity and mortality. Thus, the DASH diet can be a helpful intervention after transplantation. In a prospective cohort study of 632 adult kidney transplant recipients, greater adherence to a DASH diet was associated with a lower risk of kidney function decline (hazard ratio 0.95; P = 0.008), and also a lower risk of all-cause mortality (hazard ratio 0.95; P = 0.01).²⁸ Other studies have demonstrated similar benefits of this diet on kidney function^{4,8,9} that might be attributed to changes, similarly to the Mediterranean diet, in serum lipids, BP, insulin resistance, inflammation, oxidative stress, arterial stiffness, and endothelial function.

In conclusion, the DASH diet is an evidence-based diet to reduce sodium intake and improve BP control. A low sodium diet is already recommended for kidney transplant recipients, and the DASH diet extends this recommendation to an overall healthy eating pattern. Comparison of the Mediterranean and DASH diet is shown on Supplementary Table S2.

Vegetarian/Vegan Diet. For thousands of years, individuals have chosen to follow a vegetarian diet for religious, cultural, or ethical reasons, but it is becoming increasingly popular for overall health and well-being, including for disease treatment and prevention. There is growing evidence that reducing or eliminating meat consumption in the setting of kidney disease may delay disease progression.^{4,9}

The ability of a vegetarian diet to reduce the progression of kidney failure without impairment in clinical and nutritional status has been reported in populations around the world.^{29–33} In a cohort of 63,257 Chinese adults, red meat intake was strongly associated with ESKD risk in a dose-dependent manner, when compared with different food sources of protein.²⁹ Participants in the higher quartile of red meat consumption (~48.8 g/d) had a 40% higher risk of developing ESKD when compared with participants in the first quartile (\sim 12.5 g of red meat consumption per day), after adjusting for several covariates. Red meat and processed meat were associated with CKD risk (hazard ratio Q5 vs. Q1: 1.23, 95% confidence interval: 1.06–1.42, $P_{\text{trend}} = 0.01$) in 23-year follow-up with 2632 incident CKD cases, whereas nuts, low-fat dairy products, and legumes were protective.³⁰ In a controlled trial, elderly patients with uremia and low eGFR (5-7 ml/min) who received a vegan diet intervention with keto-analogue supplements had a delay in dialysis initiation at 1 year of follow-up.³¹ Lastly, in an observational study of 14,866 National Health and Nutrition Examination Survey participants, a higher proportion of protein from plant sources was associated with lower mortality in those with eGFR <60 ml/min per 1.73 m², and the association of plant protein intake also correlated with lower all-cause mortality in CKD.³²

There are different types of vegetarian diets. Some include animal foods like eggs and milk; others exclude any animal sources ("vegan diets"). A vegetarian diet does not necessarily signify a healthy eating pattern, and vegetarians can have processed and unhealthy food intake.³⁴ In the Atherosclerosis Risk in Communities (ARIC) study, a community-based cohort of more than 14,000 middle-aged adults with 2 semi-quantitative Food Frequency Questionnaires over 24 years of follow-up, dietary intake was assessed by plant-based diet indices, which included the quality of plantbased diet in addition to quantity in combination with the intake of animal foods.⁹ Higher adherence to a healthy plant-based diet was associated with a lower risk of CKD incidence and a slower eGFR decline when compared with participants with a less healthy plantbased diet. Thus, healthy overall dietary habits are more important than just eliminating animal-based foods.

Protein Intake: Plant-Based Versus Animal Protein

There are ongoing debates regarding whether kidney longevity means healthy vegan food and less meat or if any low-protein diet is good enough. Most relevant literature concludes that a vegetarian diet provides more quality and lower protein intake.³⁵ For patients with CKD risk factors or kidney disease, consuming foods rich in protein causes dilatation of the afferent arterioles, which increases glomerular filtration rate at a cost of higher intraglomerular pressure.³⁵ Chronic glomerular hyperfiltration as a result have consequences for long-term kidney survival, especially in the post kidney transplant population with kidney disease risk factors and lower number of nephrons. Hyperfiltration stimulates mesangial cell signaling, leading to progressive fibrosis and kidney damage. In contrast, lower intake of dietary protein leads to greater constriction of the afferent arteriole, decreasing glomerular damage and stabilizing or improving kidney function.³⁶

Patients with CKD followed for 70 months were divided into 3 groups: low-protein diet, controlled protein diet, and unrestricted protein diet, the control.³⁷ The low-protein diet patients started dialysis 24 months after the unrestricted protein diet patients (P <0.001).³⁷ In a Cochrane review, low-protein diets in nondiabetic adults delayed the progression of CKD to ESKD and dialysis initiation.³⁸ In a prospective community-based cohort of 9226 subjects, a highprotein diet was associated with a faster decline of kidney function.³⁹ Last, in 3348 women participating in the Nurses' Health Study, higher dietary intake of animal fat, such as 2 or more servings per week of red meat, was associated with an increased risk for microalbuminuria.40 The preceding studies and several others in the literature confirm the importance of a lowprotein diet in patients with CKD in preventing progression and delaying the need for renal replacement therapy.

The mechanisms by which a low-protein intake delays CKD progression include the reduced production of nitrogenous compounds that comprise uremic toxins and the lower acid load.³⁵ As the modern Western-type diet is deficient in fruits and vegetables with excessive amounts of animal foods, there is increased production of ammonia and acidogenesis leading to the loss of bone and muscle mass. A vegan dietary pattern high in fruits and vegetables favors alkalization, which improves the metabolic parameters

of acidosis, preserving bone and muscle, and slowing the glomerular filtration rate decline. 41

There are potentially favorable impacts of a vegetarian diet on minerals, such as phosphorus, potassium, and sodium control. Minerals, increasingly being used as food additives in processed, frozen, or packaged foods, were shown to contribute to dietary phosphorus and potassium loads in patients with CKD.⁴² In commonly consumed meat, poultry, and fish products, the amount of minerals is high, whereas the dietary information is not often easily accessible to the consumer. In the posttransplant context, patients tend to revert the tendency of hyperphosphatemia toward one of hypophosphatemia. However, in graft dysfunction, elevated phosphate levels is associated with increased graft loss and mortality.^{43–46} Phosphorus from plants is less well absorbed than from animal sources.⁴ In a crossover feeding trial of 2 diets (vegetarian and meat diet) in patients with CKD, the source of protein had a significant effect on phosphorus homeostasis.⁴⁷ Those following a vegetarian diet exhibited lower serum phosphorus levels, a trend toward decreased urine 24hour phosphorus excretion, and FGF23 levels, despite equivalent protein and phosphorus concentrations for both.

Most posttransplant patients do not usually need to restrict potassium. However, if they have hyperkalemia exacerbated by the effects of calcineurin inhibitors, they are warned to avoid high-potassium plant-based foods, including beans, seeds, nuts, and some fruits and vegetables. Although many plants are naturally high in potassium, their consumption influences alkalinizing effects due to intracellular potassium distribution and potassium fecal excretion related to natural fibers found in these plant-based foods.⁴ A study on restriction of high-potassium plant foods in hemodialysis patients indicated that different sources of dietary potassium are not therapeutically equivalent, and animal and plant sources of potassium may differ in their potential to contribute to hyperkalemia.⁴⁸ Although fruits and vegetables promote more benefits than risks to the potassium level, meat and processed food contribute to adverse metabolic states (e.g., oxidative stress, inflammation, metabolic acidosis, dyslipidemias) and conditions (e.g., constipation, hypertension) that negatively impact health.⁴⁹ We should simplify the dietary recommendations by asking patients to eat a variety of vegetables, fruits, grains, and less meat, processed/ packaged foods, consistent with an overall healthy dietary pattern.

Another benefit of a plant-based diet is its high fiber content, which is crucial to the gut microbiota.^{50,51} A natural diet rich in fiber in a CKD population reduced the risks of obesity, diabetes, and dyslipidemia. Moreover, it decreases the bacterial generation of uremic toxins.⁵² High dietary fiber intake is also helpful in reducing inflammation. Among 650 maintenance hemodialysis patients,⁵³ fiber intake reduced C-reactive protein, and oxidative stress, which may also impact graft survival. Although the recommended fiber intake is 25 to 35 g per day,²² most Americans consume only approximately half of the recommended intake⁵¹ and a plant-based diet might help increase its intake.

To the posttransplant kidney population, potential side effects of a vegetarian diet may exist. Vegetarianism can lead to lower intake of vitamin B12, absence of heme iron, and reduced iron absorption.⁵⁴ Eggs and dairy products represent the only natural source of vitamin B12 in a vegetarian diet, and, although the total iron content of vegetarian diets is similar to nonvegetarian diets, the bioavailability of iron is substantially lower.⁵⁴ In patients with anemia or those at risk to develop it, caution is warranted. In these cases, we recommend checking hemoglobin and iron content at least twice a year, and supplemental B12 or iron should be considered. Lastly, most of the repercussions of this diet have been studied extensively in patients with CKD⁵⁵ and little in kidney transplant recipients, and more research is needed.⁵⁶ Even with the lack of specific studies, prescribing a well-planned vegetarian diet can help manage and prevent possible health challenges in the posttransplant population, while achieving most of the nutritional requirements of patients.

Intermittent Fasting

Intermittent fasting (IF) is an increasingly adopted eating pattern. Many doctors are recommending it not only to treat obesity but also metabolic disorders. This dietary pattern is not based on specific food choices but on the timing of meals, alternating between periods of fasting and eating. There are several methods that have been tested. The most famous ones are the 16/8 method (16 hours of fasting and 8 hours of eating per day) and the 5:2 diet (5 days of normal diet followed by 2 days of restricted calorie intake of <500 kcal per day).

The main idea of IF is allowing the body to use its stored energy, by burning off excess body fat. During fasting, the available glucose stores are depleted, and triglycerides are broken into fatty acids and glycerol to produce energy. Fatty acids are converted to ketone bodies,⁵⁷ which provide not only energy but also regulate important signaling in cells, which may explain the potential benefits of this diet beyond weight reduction.

Numerous studies reported a positive association of this diet with weight loss, body fat, insulin resistance, ectopic and visceral fat stores, adipocyte size, and metabolic flexibility, with no obvious evidence of harm.⁵⁸ In mice, IF prevents metabolic diseases even in challenging situations such as in animals fed with a high-fat diet (ad libitum fed),^{59,60} and in animals with compromised metabolic dysfunction, lacking circadian clock.⁶¹ We already know that a high-fat diet, metabolic oscillations, and dysfunctions contribute to developing metabolic diseases. Thus, these mice were expected to show elevated serum glucose, serum cholesterol levels, serum triglycerides, serum leptin levels, and insulin resistance. However, the IF overrode the challenges imposed on these mice and lowered all of these factors, preventing the development of metabolic derangements. Moreover, proinflammatory cytokines, such as tumor necrosis factor- α , also decreased jointly with the decrease of the adipose tissue.^{59,61} In human studies, a lower incidence of diabetes mellitus and obesity was found in populations who usually have an IF dietary pattern, like on the island of Okinawa.⁶² Patients with prediabetes and type 2 diabetes have shown a significant impact on insulin sensitivity when fasting 3 times per week.⁶³ IF probably remodels adipose tissue and helps control all the comorbidities associated with excessive whole-body fat. This is particularly important in the transplant setting, as glucose homeostasis is disrupted in more than 75% of transplant recipients. Thus, with a high prevalence of metabolic diseases and rejection episodes in kidney transplant recipients, this dietary intervention might represent a useful tool.

However, there is no evidence-based research of IF in kidney transplant recipients. Protein intake, nutritional status, and muscle mass are also important factors to consider in the transition from ESKD to posttransplant and acutely posttransplant, protein needs are up to 1.2 g/kg. Until now there are no studies assessing the possible negative consequences of both excessive protein breakdown during fasting periods and excessive protein intake during nonfasting periods on kidney function. In addition, IF is contraindicated in patients with genetic metabolic disorders, such as carnitine deficiency (primary) and porphyria and poimbalances tential electrolyte (hypomagnesemia, hypophosphatemia).⁶⁴

Although specific trials in transplantation are needed, some studies in kidney transplant recipients during Ramadan fasting (from sunrise to sunset for 30 days) showed some promising results. No significant changes were found in serum creatinine, mean arterial pressure, urinary protein excretion and eGFR during, before, and 6 months after Ramadan in groups with low, moderate, and high eGFRs at baseline, concluding no adverse effects in the allograft function.^{65,66} Therefore, if during Ramadan, refraining from eating or drinking for 8 to 12 hours, did not have any negative side effects on kidney function in transplant recipients, we could therefore assume that the use of IF in the kidney transplant population might not have any major side effects. Nonetheless, most of the human studies are case studies or have a small sample size with a short treatment duration, which means that the potential benefits are only seen during the period of IF and may not be applicable long-term. Thus, more studies are required to determine the safety and potential benefits of IF in kidney recipients, and we do not recommend it to those patients as an initial intervention.

Low-Carb Diets

These diets are based on a low-carbohydrate intake, usually associated with high-protein and fat foods. The Paleo, South Beach, and Atkins diets are examples of low-carb diets. Here we focus on the Ketogenic diet (KD), which has emerged as a popular diet in recent years.

Ketogenic Diet. The KD normally consists of at least 70% of calories derived from fat, and less than 10% and 20% from carbs and protein, respectively. This composition is drastically different from the 2015 to 2020 US Department of Agriculture dietary recommendations²² of approximately 45% to 65% calories from carbohydrates, 20% to 35% from fat, and 10% to 35% from protein. The idea of a low-carbohydrate intake is to promote a ketosis state, in which the body primarily uses fat instead of carbohydrates to produce energy. To achieve this state, an adult needs to restrict net carbohydrate intake to as low as 20 g per day, promoting the conversion of fats into ketones.

KD is an established treatment option for reducing the frequency of seizures in children with epilepsy.^o Until now, the available literature about KD has been controversial, but the positive effects may be associated with improvements in cardiovascular risk factors, such as obesity, type 2 diabetes, and high-density lipoprotein cholesterol levels.⁶⁸ Studies analyzing KD's effect in animals of polycystic kidney disease reported a reduction in cystogenesis and cyst expansion. Ketosis strongly inhibits not only kidney cyst growth, but also inflammation and fibrosis.⁶⁹ This beneficial effect is probably mediated by the fact that during a period of energy restriction, to conserve energy and molecular resources, cells adopt a stress-resistance mode that controls many processes, including protein synthesis and inhibition of the mammalian target of rapamycin pathway, leading to lower cell proliferation and fibrosis.⁶⁹ However, these studies were in animal models and have not been translated yet to humans with polycystic kidney disease.

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In 1687 overweight and obese individuals with CKD, KD showed a positive effect on kidney function with greater increase in eGFR in the lowcarbohydrate diet group when compared with a regular diet group.⁷⁰ Another feeding trial in overweight/obese adults showed that a reduction in the glycemic index increases eGFR (P < 0.001).⁷¹ Compared with the high glycemic index/high carb diet, reducing glycemic index, % carbohydrates, or both, increased eGFR by 1.9 ml/min per 1.73 m² (95% confidence interval: 1.1–2.7; P < 0.001), 3.0 ml/min per 1.73 m² (1.9–4.0; P < 0.001), and 4.5 ml/ min per 1.73 m² (3.5–5.4; P < 0.001), respectively. Furthermore, reducing the percentage of carbohydrate intake by increasing calories from protein and fat, also increased eGFR. However, the same study highlights that replacing carbohydrates with protein can increase eGFR in the short-term and worsen kidney disease progression later. In another cohort with risk factors of kidney disease, composed of obese adults with type 2 diabetes mellitus, consumption of a low-carb and high-protein diet did not show adverse clinical effects on markers of renal function.⁷² Thus, more research is needed to conclude if the KD benefits kidney function, and caution is required in the posttransplant population, as a higher protein intake can worsen kidney function in the long-term.

Side effects of KD also exist, such as nonalcoholic fatty liver disease, insulin resistance,⁷³ and even increased mortality.⁷⁴ This diet demonstrates to be useful for the rapid induction of short-term weight loss. However, after 1 year, the KD's effects became similar to other dietary approaches, such as the Mediterranean diet, which has more scientific evidence.⁷⁵

In addition, in cultures in which carbohydrates contribute the highest amount of energy intake, it might be difficult for patients to follow this diet long-term. Prolonged compliance to KD might be associated with several limiting factors, such as high cost of foods and monotony of dietary plan, as well as physical symptoms such as halitosis and constipation. Moreover, increasing evidence shows that the quantity of carbohydrate intake is as important as quality.^{76,77} The consumption of high-quality carbohydrates (high fiber, slowly digested, and whole grains) was found to be more beneficial for cardiovascular and metabolic health outcomes than the KD,⁷⁸ especially when the KD is composed of animal-based foods and processed fats, which are notoriously unhealthy.⁷⁸ In the posttransplant context, a quality carbohydrate food choice is beneficial to combat common comorbidities, such as the incidence of posttransplant diabetes⁷⁹ and obesity,

and to reduce the side effects of immunosuppressive medications.⁸⁰ In conclusion, we recommend a diet more focused on high-quality carb intake (e.g., sweet potatoes, brown rice, beetroots, oats, quinoa, bananas) instead of restricting carbohydrate intake.

Juicing Diets

Juicing diets are becoming commonly used as a rapid way to lose weight. This diet, also called juice fast, cleanse, or detox, consists of exclusive consumption of a variety of juiced fruits and vegetables, typically for a limited time period, with low-calorie intake.⁸¹

Fruits and vegetables are rich sources of several components that contribute to general health⁸² and also have positive effects on antioxidation and immunomodulatory paths.^{83–85} Moreover, they are rich in fermentable fiber with prebiotic activity, which stimulates the growth of beneficial microorganisms (probiotics) in the gut⁸³ and have been shown to potentially help not only in the microbiota regulation^{86,87} but also in cardiovascular disease,⁸⁸ cancer,⁸⁹ obesity,^{90–92} and transplant tolerance.^{93,94} However, only 1 in 10 adults in the United States meets the amount recommended for fruits and vegetables intake,^{95,96} which should be approximately 1.5 to 2.0 cup equivalents of fruits⁹⁷ and 2.0 to 3.0 cups of vegetables per day.⁹⁸

In a recent study, 3 days of only vegetable and fruit juice diet resulted in a significant decrease in weight, lipid peroxidation, and increase in nitric oxide concentrations, which may likely contribute to cardiovascular health.⁸⁷ This diet also induced significant changes and regulation of the intestinal microbiota. The proportional of the phylum Firmicutes, which is correlated with obesity and immune dysregulation, was significantly decreased, although the phylum Bacteroidetes was significantly increased. Bacteroidetes have been associated with higher cardiovascular health, reduced obesity, and regulation of inflammatory paths that could be helpful to improve transplant outcomes.^{93,94,99–104}

Although there are potential positive impacts on the overall health of patients with CKD, caution is necessary, because fruits and vegetables are high in oxalate, which is a potential nephrotoxin and can cause oxalate nephropathy.^{105–107} There are also concerns of juicing with the possible increased risk of hyperkalemia as well as excessive vitamin C and vitamin K intake. For patients taking blood thinners, such as warfarin, a high dietary intake of vitamin K can lead to increased clotting of the blood.¹⁰⁵ In the posttransplant population, some fruits, such as grapefruit, should be avoided because of interaction with immunosuppressive drugs.¹⁰⁸ There is also concern in this immunosuppressed population about food safety of fresh juices,

and we recommend pasteurization of them when not made at home.

In addition, some types of juices (cold-pressed) do not contain fiber, which could lead to constipation. It is also difficult to conclude that juicing is healthier than eating whole fruits and vegetables. However, in a population with insufficient fruit and vegetable intake, juicing with extracts from fresh fruits and vegetables can be an easy way to increase their consumption and meet the amount recommended.

To sum up, this diet may show benefits when compared with other diets, as it lowers weight and recovers the balance of the gut microbiota in a short period of time, which could be helpful for the regulation of inflammatory paths that impact transplant outcomes. For a patient who does not enjoy eating fruits and vegetables, juicing may be a way to provide nutrients that would be missing. Otherwise, we suggest having a balanced smoothie, mixing a variety of fruits and vegetables as part of a meal or snack and if the patient chooses to try a juicing diet, we recommend following it for a short time.

Conclusion

After reviewing the literature, we conclude that the Mediterranean and the DASH diets are the most beneficial dietary patterns in the post kidney transplant population. They focus on less meat and processed food, and more fresh food and plant-based choices. We have also highlighted that single-nutrient interventions are probably less effective than a dietary pattern intervention for improving health, such as graft and patient survival after kidney transplantation. In addition, we believe that to obtain a posttransplant healthy lifestyle, patients should choose a dietary pattern that is sustainable long-term. To translate the most recent scientific evidence-based recommendations into clinical practice, we built, in a creative way, a table (Supplementary Table S3) with practical advice for each diet and an illustration (Figure 1) with suggestions of food groups and healthy meal preparations for kidney transplant recipients.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Table S1. Healthy Mediterranean-style eating pattern: rec-ommended amounts of food from each food group at 12calorie levels.

Table S2. Comparison of Dietary Approaches to StopHypertension (DASH) and Mediterranean diets.

Table S3. Practical advice of different dietary trends for transplant recipients.

REFERENCES

- Orlich MJ, Singh PN, Sabaté J, et al. Vegetarian dietary patterns and mortality in Adventist Health Study 2. JAMA Intern Med. 2013;173:1230–1238.
- What is a plant-based diet , and is it good for your kidneys ? National Kidney Foundation Web site. Updated August 18, 2018. Available at: https://www.kidney.org/atoz/content/whatplant-based-diet-and-it-good-kidney-disease. Accessed January 21, 2021.
- van Westing AC, Küpers LK, Geleijnse JM. Diet and kidney function: a literature review. *Curr Hypertens Rep.* 2020;22:1–9.
- Clegg DJ, Gallant KMH. Plant-based diets in CKD. *Clin J Am* Soc Nephrol. 2019;14:141–143.
- Wai SN, Kelly JT, Johnson DW, Campbell KL. Dietary patterns and clinical outcomes in chronic kidney disease: The CKD.OLD Nutrition Study. J Ren Nutr. 2017;27:175–182.
- Nettleton JA, Steffen LM, Palmas W, et al. Associations between microalbuminuria and animal foods, plant foods, and dietary patterns in the Multiethnic Study of Atherosclerosis. *Am J Clin Nutr.* 2008;87:1825–1836.
- Banerjee T, Crews DC, Wesson DE, et al. High dietary acid load predicts ESRD among adults with CKD. J Am Soc Nephrol. 2015;26:1693–1700.
- Gutiérrez OM, Muntner P, Rizk DV, et al. Dietary patterns and risk of death and progression to ESRD in individuals with CKD: a cohort study. *Am J Kidney Dis.* 2014;64:204–213.
- Kim H, Caulfield LE, Garcia-Larsen V, et al. Plant-based diets and incident CKD and kidney function. *Clin J Am Soc Nephrol.* 2019;14:682–691.
- Stamler J. Toward a modern Mediterranean diet for the 21st century. Nutr Metab Cardiovasc Dis. 2013;23:1159–1162.
- Sofi F, Abbate R, Gensini GF, Casini A. Accruing evidence on benefits of adherence to the Mediterranean diet on health: an updated systematic review and meta-analysis. *Am J Clin Nutr.* 2010;92:1189–1196.
- Gomes-Neto AW, Osté MCJ, Sotomayor CG, et al. Mediterranean style diet and kidney function loss in kidney transplant recipients. *Clin J Am Soc Nephrol.* 2020;15:238–246.
- Bach KE, Kelly JT, Campbell KL, et al. Healthy dietary patterns and incidence of CKD: A meta-analysis of cohort studies. *Clin J Am Soc Nephrol.* 2019;14:1441–1449.
- Chauveau P, Aparicio M, Bellizzi V, et al. Mediterranean diet as the diet of choice for patients with chronic kidney disease. *Nephrol Dial Transplant.* 2018;33:725–735.
- Khatri M, Moon YP, Scarmeas N, et al. The association between a mediterranean-style diet and kidney function in the northern manhattan study cohort. *Clin J Am Soc Nephrol.* 2014;9:1868–1875.
- Stachowska E, Wesołowska T, Olszewska M, et al. Elements of Mediterranean diet improve oxidative status in blood of kidney graft recipients. *Br J Nutr.* 2005;93:345–352.
- Schwingshackl L, Hoffmann G. Mediterranean dietary pattern, inflammation and endothelial function: a systematic review and meta-analysis of intervention trials. *Nutr Metab Cardiovasc Dis.* 2014;24:929–939.
- Minelli P, Montinari MR. The Mediterranean diet and cardioprotection: historical overview and current research. *J Multidiscip Healthc*. 2019;12:805–815.

- Martínez-González MA, Gea A, Ruiz-Canela M. The Mediterranean diet and cardiovascular health. *Circ Res.* 2019;124: 779–798.
- U.S. Department of Agriculture, Agricultural Research Service. Nutrient intakes from food and beverages: mean amounts consumed per individual, by gender and age, what we eat in America, NHANES 2013–2014. Available at: www.ars.usda.gov/nea/bhnrc/fsrg. Accessed January 21, 2021.
- 21. Slavin J. Dietary guidelines. Nutr Today. 2012;47:245-251.
- U.S. Department of Health and Human Services and U.S. Department of Agriculture. 2015–2020 Dietary Guidelines for Americans. 8th Edition. Published December 2015. Available at: https://health.gov/our-work/food-nutrition/previous-dietaryguidelines/2015. Accessed September 4, 2020.
- Safa K, Ohori S, Borges TJ, et al. Salt accelerates allograft rejection through serum- and glucocorticoid-regulated kinase-1-dependent inhibition of regulatory T cells. J Am Soc Nephrol. 2015;26:2341–2347.
- Siervo M, Lara J, Chowdhury S, et al. Effects of the Dietary Approach to Stop Hypertension (DASH) diet on cardiovascular risk factors: a systematic review and meta-analysis. *Br J Nutr.* 2015;113:1–15.
- Appel LJ, Moore TJ, Obarzanek E, et al. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med.* 1997;336:1117–1124.
- Hollenberg NK. Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet: Editor's comments. *Curr Hypertens Rep.* 2001;3:373.
- Weir MR, Burgess ED, Cooper JE, et al. Assessment and management of hypertension in transplant patients. *J Am Soc Nephrol.* 2015;26:1248–1260.
- Osté MCJ, Gomes-Neto AW, Corpeleijn E, et al. Dietary Approach to Stop Hypertension (DASH) diet and risk of renal function decline and all-cause mortality in renal transplant recipients. *Am J Transplant.* 2018;18:2523–2533.
- 29. Lew QLJ, Jafar TH, Koh HWL, et al. Red meat intake and risk of ESRD. *J Am Soc Nephrol.* 2017;28:304–312.
- **30.** Haring B, Selvin E, Liang M, et al. Dietary protein sources and risk for incident chronic kidney disease: results from the Atherosclerosis Risk in Communities (ARIC) Study. *J Ren Nutr.* 2017;27:233–242.
- **31.** Brunori G, Viola BF, Parrinello G, et al. Efficacy and safety of a very-low-protein diet when postponing dialysis in the elderly: a prospective randomized multicenter controlled study. *Am J Kidney Dis.* 2007;49:569–580.
- **32.** Chen X, Wei G, Jalili T, et al. The associations of plant protein intake with all-cause mortality in CKD. *Am J Kidney Dis.* 2016;67:423–430.
- **33.** Wiwanitkit V. Renal function parameters of Thai vegans compared with non-vegans. *Ren Fail*. 2007;29:219–220.
- Plant-Based Diet or Vegetarian Diet What is the Difference? | National Kidney Foundation Web site. Available at: https:// www.kidney.org/atoz/content/plant-based-diet-or-vegetariandiet-difference. Accessed May 14, 2020.
- Kalantar-Zadeh K, Moore LW. Does kidney longevity mean healthy vegan food and less meat or is any low-protein diet good enough? *J Ren Nutr.* 2019;29:79–81.

- Kalantar-Zadeh K, Fouque D. Nutritional management of chronic kidney disease. N Engl J Med. 2017;377:1765–1776.
- Baragetti I, De Simone I, Biazzi C, et al. The low-protein diet for chronic kidney disease: 8 years of clinical experience in a nephrology ward. *Clin Kidney J.* 2019;13:253–260.
- Hahn D, Hodson EM, Fouque D. Low protein diets for nondiabetic adults with chronic kidney disease. *Cochrane Database Syst Rev.* 2018;10:CD001892.
- **39.** Jhee JH, Kee YK, Park S, et al. High-protein diet with renal hyperfiltration is associated with rapid decline rate of renal function: a community-based prospective cohort study. *Nephrol Dial Transplant.* 2020;35:98–106.
- Lin J, Hu FB, Curhan GC. Associations of diet with albuminuria and kidney function decline. *Clin J Am Soc Nephrol.* 2010;5:836–843.
- Rodrigues Neto Angéloco L, Arces de Souza GC, Almeida Romão E, Garcia Chiarello P. Alkaline diet and metabolic acidosis: practical approaches to the nutritional management of chronic kidney disease. *J Ren Nutr.* 2018;28:215– 220.
- Parpia AS, L'Abbé M, Goldstein M, et al. The impact of additives on the phosphorus, potassium, and sodium content of commonly consumed meat, poultry, and fish products among patients with chronic kidney disease. *J Ren Nutr.* 2018;28:83–90.
- **43.** Jeon HJ, Kim YC, Park S, et al. Association of serum phosphorus concentration with mortality and graft failure among kidney transplant recipients. *Clin J Am Soc Nephrol.* 2017;12:653–662.
- 44. Van Londen M, Aarts BM, Deetman PE, et al. Post-transplant hypophosphatemia and the risk of death-censored graft failure and mortality after kidney transplantation. *Clin J Am Soc Nephrol.* 2017;12:1301–1310.
- Connolly GM, Cunningham R, McNamee PT, et al. Elevated serum phosphate predicts mortality in renal transplant recipients. *Transplantation*. 2009;87:1040–1044.
- **46.** Stevens KK, Morgan IR, Patel RK, et al. Serum phosphate and outcome at one year after deceased donor renal transplantation. *Clin Transplant.* 2011;25:E199–E204.
- Moe SM, Zidehsarai MP, Chambers MA, et al. Vegetarian compared with meat dietary protein source and phosphorus homeostasis in chronic kidney disease. *Clin J Am Soc Nephrol.* 2011;6:257–264.
- St-Jules DE, Goldfarb DS, Sevick MA. Nutrient nonequivalence: does restricting high-potassium plant foods help to prevent hyperkalemia in hemodialysis patients? [published correction appears in J Ren Nutr. 2016 Nov;26(6): 416] *J Ren Nutr.* 2016;26:282–287.
- Noori N, Kalantar-Zadeh K, Kovesdy CP, et al. Dietary potassium intake and mortality in long-term hemodialysis patients. *Am J Kidney Dis.* 2010;56:338–347.
- 50. Black AP, Anjos JS, Cardozo L, et al. Does low-protein diet influence the uremic toxin serum levels from the gut microbiota in nondialysis chronic kidney disease patients? *J Ren Nutr.* 2018;28:208–214.
- Recommended Daily Intake. Fiber Facts.org Web site. Updated January 23, 2017. Available at: https://www. fiberfacts.org/hcp-recommended-daily-intake/. Accessed September 18, 2020.

- Camerotto C, Cupisti A, D'Alessandro C, et al. Dietary fiber and gut microbiota in renal diets. *Nutrients*. 2019;11:1–15.
- **53.** Demirci BG, Tutal E, Eminsoy IO, et al. Dietary fiber intake: its relation with glycation end products and arterial stiffness in end-stage renal disease patients. *J Ren Nutr.* 2019;29:136– 142.
- Chauveau P, Combe C, Fouque D, Aparicio M. Vegetarianism: advantages and drawbacks in patients with chronic kidney diseases. *J Ren Nutr.* 2013;23:399–405.
- Joshi S, Shah S, Kalantar-Zadeh K. Adequacy of plant-based proteins in chronic kidney disease. J Ren Nutr. 2019;29:112– 117.
- **56.** Nolte Fong JV, Moore LW. Nutrition trends in kidney transplant recipients: the importance of dietary monitoring and need for evidence-based recommendations. *Front Med.* 2018;5:302.
- De Cabo R, Mattson MP. Effects of intermittent fasting on health, aging, and disease. N Engl J Med. 2019;381:2541– 2551.
- Harvie M, Howell A. Potential benefits and harms of intermittent energy restriction and intermittent fasting amongst obese, overweight and normal weight subjects-A narrative review of human and animal evidence. *Behav Sci (Basel)*. 2017;7:4.
- Hatori M, Vollmers C, Zarrinpar A, et al. Time-restricted feeding without reducing caloric intake prevents metabolic diseases in mice fed a high-fat diet. *Cell Metab.* 2012;15:848– 860.
- Chaix A, Zarrinpar A, Miu P, Panda S. Time-restricted feeding is a preventative and therapeutic intervention against diverse nutritional challenges. *Cell Metab.* 2014;20: 991–1005.
- Chaix A, Lin T, Le HD, et al. Time-restricted feeding prevents obesity and metabolic syndrome in mice lacking a circadian clock. *Cell Metab.* 2019;29:303–319.e4.
- Willcox DC, Willcox BJ, Todoriki H, et al. Caloric restriction and human longevity: What can we learn from the Okinawans? *Biogerontology*. 2006;7:173–177.
- Furmli S, Elmasry R, Ramos M, Fung J. Therapeutic use of intermittent fasting for people with type 2 diabetes as an alternative to insulin. *BMJ Case Rep.* 2018;2018:2017221854.
- Kossoff EH, Zupec-Kania BA, Auvin S, et al. Optimal clinical management of children receiving dietary therapies for epilepsy: updated recommendations of the International Ketogenic Diet Study Group. *Epilepsia Open*. 2018;3:175– 192.
- 65. Qurashi S, Tamimi A, Jaradat M, Al Sayyari A. Effect of fasting for Ramadan on kidney graft function during the hottest month of the year (August) in Riyadh, Saudi Arabia. *Exp Clin Transplant.* 2012;10:551–553.
- Ghalib M, Qureshi J, Tamim H, et al. Does repeated Ramadan fasting adversely affect kidney function in renal transplant patients? *Transplantation*. 2008;85:141–144.
- Ketogenic diet. Epilepsy Society Web site. Updated April 2019. Available at: https://www.epilepsysociety.org.uk/ ketogenic-diet. Accessed September 4, 2020.
- Kosinski C, Jornayvaz FR. Effects of ketogenic diets on cardiovascular risk factors: evidence from animal and human studies. *Nutrients*. 2017;9:1–16.

- **69.** Torres JA, Kruger SL, Broderick C, et al. Ketosis ameliorates renal cyst growth in polycystic kidney disease. *Cell Metab.* 2019;30:1007–1023.e5.
- Oyabu C, Hashimoto Y, Fukuda T, et al. Impact of lowcarbohydrate diet on renal function: a meta-analysis of over 1000 individuals from nine randomised controlled trials. *Br J Nutr.* 2016;116:632–638.
- Juraschek SP, Chang AR, Appel LJ, et al. Effect of glycemic index and carbohydrate intake on kidney function in healthy adults. *BMC Nephrol.* 2016;17:70.
- 72. Tay J, Thompson CH, Luscombe-Marsh ND, et al. Long-term effects of a very low carbohydrate compared with a high carbohydrate diet on renal function in individuals with type 2 diabetes: a randomized trial. *Medicine (Baltimore)*. 2015;94, e2181.
- 73. Ellenbroek JH, van Dijck L, Töns HA, et al. Long-term ketogenic diet causes glucose intolerance and reduced β- and αcell mass but no weight loss in mice. Am J Physiol Endocrinol Metab. 2014;306:E552–E558.
- Seidelmann SB, Claggett B, Cheng S, et al. Dietary carbohydrate intake and mortality: a prospective cohort study and meta-analysis. *Lancet Public Health*. 2018;3:e419–e428.
- Bravata DM, Sanders L, Huang J, et al. Efficacy and safety of low-carbohydrate diets: a systematic review. JAMA. 2003;289:1837–1850.
- Ludwig DS, Hu FB, Tappy L, Brand-Miller J. Dietary carbohydrates: role of quality and quantity in chronic disease. *BMJ*. 2018;361:k2340.
- Reynolds A, Mann J, Cummings J, et al. Carbohydrate quality and human health: a series of systematic reviews and meta-analyses [published correction appears in Lancet. 2019 Feb 2;393(10170):406] *Lancet*. 2019;393: 434–445.
- Giugliano D, Maiorino MI, Bellastella G, Esposito K. More sugar? No, thank you! The elusive nature of low carbohydrate diets. *Endocrine*. 2018;61:383–387.
- Sharif A, Moore R, Baboolal K. Influence of lifestyle modification in renal transplant recipients with postprandial hyperglycemia. *Transplantation*. 2008;85:353–358.
- Wissing KM, Pipeleers L. Obesity, metabolic syndrome and diabetes mellitus after renal transplantation: prevention and treatment. *Transplant Rev.* 2014;28:37–46.
- What is a juice diet? BBC Good Food Web site. Available at: https://www.bbcgoodfood.com/howto/guide/what-juice-diet. Accessed June 29, 2020.
- U.S. Department. of Agriculture, Center for Nutrition Policy and Promotion. MyPlate Dairy Group. Nutrients and health benefits. ChooseMyPlate.gov. Published 2015. Available at: https://www.choosemyplate.gov/eathealthy/fruits/fruitsnutrients-health. Accessed January 22, 2020.
- Abuajah CI, Ogbonna AC, Osuji CM. Functional components and medicinal properties of food: a review. *J Food Sci Technol.* 2015;52:2522–2529.
- Yahfoufi N, Alsadi N, Jambi M, Matar C. The immunomodulatory and anti-inflammatory role of polyphenols. *Nutrients*. 2018;10:1–23.
- 85. Hussain T, Tan B, Yin Y, et al. Oxidative stress and inflammation: what polyphenols can do for us? *Oxid Med Cell Longev.* 2016;2016:7432797.

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- Simpson HL, Campbell BJ. Review article: Dietary fibremicrobiota interactions. *Aliment Pharmacol Ther.* 2015;42: 158–179.
- Henning SM, Yang J, Shao P, et al. Health benefit of vegetable/fruit juice-based diet: Role of microbiome. *Sci Rep.* 2017;7:2167.
- Tomé-Carneiro J, Visioli F. Polyphenol-based nutraceuticals for the prevention and treatment of cardiovascular disease: Review of human evidence. *Phytomedicine*. 2016;23:1145–1174.
- **89.** Paul B, Barnes S, Demark-Wahnefried W, et al. Influences of diet and the gut microbiome on epigenetic modulation in cancer and other diseases. *Clin Epigenetics*. 2015;7:112.
- 90. Muscogiuri G, Cantone E, Cassarano S, et al. Gut microbiota: a new path to treat obesity. *Int J Obes Suppl*. 2019;9:10–19.
- **91.** Castaner O, Goday A, Park YM, et al. The gut microbiome profile in obesity: a systematic review. *Int J Endocrinol.* 2018;2018:4095789.
- 92. Kvit KB, Kharchenko NV. Gut microbiota changes as a risk factor for obesity. *Wiad Lek*. 2017;70:231–235.
- 93. Wu H, Singer J, Kwan TK, et al. Gut microbial metabolites induce donor-specific tolerance of kidney allografts through induction of T regulatory cells by short-chain fatty acids. *J Am Soc Nephrol.* 2020;31:1445–1461.
- 94. Alegre M-L. Can diet induce transplantation tolerance? *J Am Soc Nephrol.* 2020;31:1417–1418.
- 95. Centers for Disease Control and Prevention. Only 1 in 10 adults get enough fruits or vegetables. CDC.gov. Updated November 16, 2017. Available at: https://www.cdc.gov/ media/releases/2017/p1116-fruit-vegetable-consumption. html. Accessed June 29, 2020.
- 96. Lee-Kwan SH, Moore LV, Blanck HM, et al. Disparities in state-specific adult fruit and vegetable consumption – United States, 2015. *MMWR Morb Mortal Wkly Rep.* 2017;66:1241–1247.
- U.S. Department of Agriculture, Center for Nutrition Policy and Promotion. All about the fruit group. ChooseMyPlate.gov. Published 2015. Available at: https://www.choosemyplate.gov/ eathealthy/fruits. Accessed June 29, 2020.
- U.S. Department of Agriculture, Center for Nutrition Policy and Promotion. All about the vegetable group. ChooseMyPlate. gov. Published 2015. Available at: https://www.choosemyplate. gov/eathealthy/vegetables. Accessed June 29, 2020.

- Sepulveda M, Pirozzolo I, Alegre ML. Impact of the microbiota on solid organ transplant rejection. *Curr Opin Organ Transplant*. 2019;24:679–686.
- A-344 Influence of the Gut Microbiota on Acute Rejection of Vascular Allografts (ID 291) - 2020 American Transplant Congress. Available at: https://virtualmeeting.ctimeetingtech. com/atc/attendee/eposter/poster/291?q=microbiota. Accessed June 30, 2020.
- The gut microbiota stimulates dendritic cells for immune modulation - ATC Abstracts. Available at: https:// atcmeetingabstracts.com/abstract/the-gut-microbiota-stimulatesdendritic-cells-for-immune-modulation/. Accessed June 30, 2020.
- 102. Changes in gut microbiota and acute rejection after kidney transplantation - ATC Abstracts. Available at: https:// atcmeetingabstracts.com/abstract/changes-in-gut-microbiotaand-acute-rejection-after-kidney-transplantation/. Accessed June 30, 2020.
- 103. Specific gut microbiota community suppresses acute rejection by reducing natural killer cell population - ATC Abstracts. Available at: https://atcmeetingabstracts.com/abstract/specificgut-microbiota-community-suppresses-acute-rejectionby-reducing-natural-killer-cell-population/. Accessed June 30, 2020.
- 104. Microbiota modulates ischemia-reperfusion injury in mouse liver transplantation - ATC Abstracts. Available at: https:// atcmeetingabstracts.com/abstract/microbiota-modulatesischemia-reperfusion-injury-in-mouse-liver-transplantation/. Accessed June 30, 2020.
- Ulerich L. To juice or not to juice? National Kidney Foundation Web site. Published October 12, 2018. Available at: https://www.kidney.org/content/juice-or-not-juice. Accessed June 29, 2020.
- 106. Lien YHH. Juicing is not all juicy. *Am J Med.* 2013;126:755–756.
- 107. Getting JE, Gregoire JR, Phul A, Kasten MJ. Oxalate nephropathy due to "juicing": case report and review. *Am J Med.* 2013;126:768–772.
- 108. Auten AA, Beauchamp LN, Taylor J, et al. Hidden sources of grapefruit in beverages: potential interactions with immunosuppressant medications. *Hosp Pharm.* 2013;48: 489–493.