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Cardiovascular disease risk factors and lifestyle modification strategies after pediatric kidney transplantation: what are we dealing with, and what can we target?

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Abstract

Kidney transplantation in pediatric patients can lead to partial improvement of some of the cardiometabolic parameters that increase the risk for cardiovascular disease (CVD) in patients with chronic kidney disease. However, even after restoration of kidney function, transplant recipients remain at risk for CVD due to the continual presence of traditional and non-traditional risk factors, including the side effects of immunosuppression and chronic inflammation. This educational review describes the prevalence of CVD risk factors in pediatric kidney transplant recipients and presents available evidence for therapeutic lifestyle changes and other non-pharmacologic strategies that can be used to improve traditional and modifiable CVD risk factors. Although trial-grade evidence for interventions that improve CVD in pediatric kidney transplant recipients is limited, potential strategies include lowering dietary sodium and saturated fat intake and increasing physical activity levels. Intensive follow-up may help patients achieve guideline-recommended goals for reducing their overall CVD risk.

Keywords

Pediatric; Kidney; Transplant; Obesity; Hypertension; Dyslipidemia

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Introduction

For pediatric kidney transplant recipients (KTRs), life expectancy after transplantation has improved significantly in the past 30 years with advances in immunosuppression, treatment of acute rejection, and infection control [1]. Cardiovascular disease (CVD) remains the leading cause of death not only for children with kidney failure, but also for pediatric KTRs, accounting for an estimated 35–40% of KTR mortality [2, 3]. Pediatric KTRs are at particularly high risk for the development or exacerbation of comorbid conditions such as dyslipidemia, hypertension, insulin resistance, metabolic syndrome, and diabetes.

Although some of the CVD risk factors associated with chronic kidney disease (CKD) or dialysis—such as azotemia, anemia, fluid overload, CKD mineral and bone disorder, and chronic inflammation—can improve with kidney transplantation, over half of pediatric KTRs will have at least one persistent or new-onset cardiovascular risk factor in the year following kidney transplantation. Reasons for the high CVD risk in pediatric KTRs include exposure to immunosuppression-related side effects, steroids, weight gain with improved appetite, and physical inactivity [4, 5]. Persistence of CKD-related comorbidities including anemia, proteinuria, and hyperparathyroidism may also further contribute to the increased CVD risk of pediatric KTRs.

Lack of long-term pediatric data that tracks outcomes from childhood into late adulthood makes mitigating cardiovascular risk challenging when there are few interventional studies to inform guidelines. Given the long duration of time it may take for the burden of atherosclerotic disease to accumulate and lead to the onset of “hard” outcomes (e.g., myocardial infarction, stroke) in later adulthood, reliance on surrogate markers of CVD, including the presence of left ventricular hypertrophy, increased carotid intima-media thickness (cIMT) and coronary calcification [6], is common in younger populations. However, even after kidney transplantation, left ventricular hypertrophy and abnormal cIMT often persist [6, 7], suggesting that these factors do not necessarily regress with transplantation.

The current review will focus primarily on the available data for lifestyle interventions that can be used to address CVD risk factors including hypertension, obesity and physical inactivity, insulin resistance, and dyslipidemia. Pharmacologic strategies to ameliorate immunosuppression-related side effect profiles have been described previously and will not be the focus of this review [4, 5, 8]. Existing guidelines for lifestyle recommendations for children with other high-risk pediatric health conditions and adult KTRs that may be broadly applicable to the pediatric KTR population are summarized in Table 1.

Lifestyle interventions that address hypertension

There are numerous factors contributing to the persistence or onset of hypertension after kidney transplantation including the use of immunosuppressive agents such as calcineurin inhibitors which can increase blood pressure (BP), exposure to steroids, weight gain with improved appetite, and presence of renal artery stenosis within the allograft [18–20]. It is estimated that the prevalence of hypertension in pediatric KTRs is 60–90% [6, 18, 21–23] and an estimated 31–61% of KTRs with hypertension continue to have poorly controlled BP [21–23].

Among pediatric KTRs, one study found that every 10% increase in systolic BP was associated with a twofold higher risk for subsequent graft failure within 1 year of transplantation [24]. Similarly, in adult KTRs, every 20-mmHg increase in systolic BP was associated with a 32% increase in subsequent CVD risk [25]. The impact of lifestyle interventions on hypertension control in pediatric KTRs has not been directly tested in large clinical trials. Most data on the management of hypertension in children are extrapolated from adults. A study of adult KTRs in Japan found that 3 sessions of monthly to bimonthly dietary counseling on reducing salt intake resulted in nearly a quarter of participants successfully weaning or discontinuing antihypertensive medication due to improved systolic BP. The intervention also helped reduce sodium intake (ascertained by 24-h urinary sodium excretion), although the long-term sustainability of the effects of this intervention is unclear [26].

The Dietary Approaches to Stop Hypertension (DASH) diet recommends increasing the intake of fruits, vegetables, whole grains, legumes, nuts, and low-fat dairy products while reducing sugar-sweetened beverage and red meat consumption. A prospective observational study previously evaluated the association between adherence to the DASH diet and kidney function and mortality in adult KTRs. Participants were asked to complete food frequency questionnaires, and their diets were rated by level of adherence to the DASH diet. Subjects were followed prospectively for a median of 5.3 years. In this study, greater adherence to the DASH diet at baseline was associated with lower risk of kidney function decline and all-cause mortality, even after adjustment for baseline systolic BP and use of antihypertensive drugs [27].

The DASH diet has also been associated with reductions in BP, improved fasting glucose levels, and improved abdominal obesity in the general pediatric population [28], but this has not been examined specifically in children with a functional allograft. A prior randomized controlled trial was performed to evaluate the efficacy of a DASH intervention for adolescents with elevated BP or hypertension, but without kidney disease, over a 3-month period. The intervention involved recommendations for dietary changes; a 60-min counseling session between a dietitian, the adolescent, and their parent; and a total of 10 phone calls with trained interventionists. Compared with routine care, adolescents assigned to the DASH diet lowered their systolic BP by an average of 8 mmHg more than the usual care group by the end of the intervention period [29], but the effect was not sustained after the end of the trial. Although access to intensive dietary counseling itself in this intervention may have contributed to the positive effects of the DASH diet, this is one of the few randomized controlled trials demonstrating the feasibility of implementing a DASH diet for improving shorter-term BP control in children.

Vegetarian and plant-based diets have garnered attention in the treatment of adults with CKD due to their potential to lower BP and reduce inflammation. Such diets are also typically lower in sodium, acid, and phosphate load and have higher fiber content [30–33] and thus may have multiple benefits with regard to cardiovascular health. Plant-based diets have been suggested as a strategy for reducing CVD risk in children [34], but the feasibility of implementing such diets in growing children, and particularly those with CKD or a functional allograft, is less well-established than for adults. In theory, children following vegetarian and vegan diets may be at risk for nutritional deficiencies or inadequate protein intake [35], but this risk may be mitigated among pediatric KTRs given frequent follow-up and the availability of dietitian support in most clinic settings.

In one trial, 30 pediatric patients with hypercholesterolemia and obesity (but without kidney disease) and their parents were randomized and received education to institute either the American Heart Association (AHA) or a plant-based diet over 4 weeks [36]. Both diets led to improvements in objective markers of CVD risk (modest reductions in systolic BP, inflammatory markers, weight, and insulin levels). The plant-based diet had a more pronounced benefit than the AHA diet in terms of lowering cholesterol. Of note, the only significant barrier to changing the family's diet was that parents reported more challenges in purchasing plant-based foods, as compared to foods recommended in the AHA diet [36]. Many adult and pediatric nephrologists and dietitians endorse the benefits of plant-based diets for CKD management, but providers may not feel confident in their ability to successfully transition a patient to a fully plant-based diet while balancing essential nutrient intake [37]. Although there is evidence to suggest that these diets are beneficial for adults with CKD [30, 33], no studies to our knowledge have specifically evaluated these diets in KTRs (see Table 2).

Lifestyle interventions that address physical inactivity and obesity

After transplantation, excessive and early weight gain is common [38] and can persist into adulthood [39]. Weight gain after kidney transplantation may be related to improved appetite, steroid use, or persistence of low physical activity levels. A longitudinal study in the UK revealed that the prevalence of being overweight or obese increased from 31% before transplantation to 53% after transplantation. The greatest increase in weight occurred in the initial 4 months after kidney transplantation, with high BMI pre-transplantation being an important risk factor for persistent obesity [40].

In pediatric patients with high cardiovascular risk, which includes pediatric KTRs, the AHA recommends at least 5 h of moderate to vigorous physical activity weekly, with counseling on achieving this goal at each health encounter [10]. Low levels of self-reported physical activity have been described among pediatric KTRs. A study of 60 pediatric and young adult KTRs in Israel found that 50% of respondents reported no regular physical activity at all [41]. A study of 25 pediatric KTRs and 15 children on dialysis in the USA used the Previous Day Physical Activity Recall to capture activity levels and the perceived level of exertion for each activity [42]. Both KTRs and those on dialysis spent less than 10% of non-school time engaged in physical activity. Furthermore, there was no difference between those treated with dialysis or kidney transplantation, even though KTRs theoretically should have improved capacity to participate in physical activity [42]. Similarly, a cross-sectional study using the Physical Activity Questionnaire found that 6 months after transplantation, despite two-thirds of KTRs reporting increased activity levels, physical activity remained lower in pediatric KTRs than in healthy children [43]. After transplantation, many recipients may be more concerned about their exercise limitations (i.e., in the setting of a solitary functional kidney) than the benefits of regular exercise [43].

Although self- or parent-reported physical activity levels may be subject to inaccuracies, objective measures also confirm a high prevalence of physical inactivity among pediatric KTRs. A study using accelerometry data over 3 days showed that among 16 pediatric KTRs in Canada, 59% spent their free time in sedentary activities and low-intensity exercise, and participants had poor exercise capacity and physical fitness [44]. Similarly, a study of 16 pediatric KTRs in the USA found that at least 3–5 h of physical exercise per week was necessary in this population to attain cardiorespiratory fitness levels comparable to healthy controls with sedentary lifestyles who exercised less than 3 h per week [45]. Although the recommended number of steps per day is 15,000 and 12,000 for males and females, respectively, for healthy children 6–12 years of age [46], the median step count of children with CKD, kidney failure, and KTRs in one study was less than half of the recommended activity level at just under 6000 steps per day [47].

Interventions to improve physical activity have been tested in trial settings in children with CKD and kidney failure but have had variable effects. A 12-week pedometer-based intervention in children with CKD, kidney failure, and KTRs which aimed to increase average daily step counts to recommended targets with weekly feedback did not have any effect on average daily step counts [47]. However, KTRs, as opposed to those with earlier-stage CKD or on dialysis, who increased their daily step counts by more than 1000 steps per day were observed to improve their performance during a 6-min walk test, providing evidence that fitness can improve over time in this specific subgroup. A school-based study using pedometers among healthy children in the UK found that children who received a daily step count goal (and were given a reward if they achieved this goal) had the largest increase in daily step counts, as compared to those with a step count goal but no rewards or to the control group who received neither a goal nor a reward [48]. Thus, incentivizing physical activity may be important to increase physical activity among all children.

Home-based exercise interventions via active videogaming or “exergaming” have also been tested as means of improving cardiorespiratory fitness, motor coordination, and overall health. In one 6-week study, KTRs 8–21 years of age were given Nintendo *Wii*® game consoles and asked to play Wii Fit for three 30-min sessions per week while wearing a heart rate monitor [49]. There was low compliance with exergaming and inadequately achieved physical activity levels based on heart rate monitoring data. Despite the low compliance, steps per hour significantly increased after 6 weeks of exergaming. Although active videogaming did not improve cardiorespiratory fitness, the authors proposed it may have served as a stimulus for increasing physical activity.

One study observed the effects of annual dietary counseling that was customized to the needs of pediatric KTRs in accordance with the Practice Guideline for Nutrition in Children with CKD [38]. This study found that annual dietary counseling alone was not associated with less weight gain by 2 years after transplant, and the prevalence of obesity had increased from 14 to 43%, with most of the weight gain occurring in the first 6 months after transplantation. The authors suggested that more frequent dietitian evaluation and counseling may be necessary to prevent weight gain in children after kidney transplantation. However, many dietary and lifestyle interventions are challenging to implement in daily clinical practice due to poor adherence, especially among adolescents, and adherence to immunosuppression may take priority over dietary and lifestyle changes. Future research is needed to determine how to encourage adherence to dietary interventions in the KTR population.

Lifestyle interventions that address insulin resistance

The prevalence of insulin resistance and metabolic syndrome is known to be elevated in patients with CKD [50], but this risk is heightened after kidney transplantation and exacerbated by the side effect profiles of immunosuppressive agents [4, 5]. Corticosteroids, tacrolimus, cyclosporine, and mammalian target of rapamycin (mTOR) inhibitors all have potential to induce hyperglycemia or new-onset diabetes.

In a retrospective study of over 200 pediatric KTRs in the USA, the prevalence of metabolic syndrome increased from 19% at the time of transplant to 37% 1 year after transplantation [51]. In a review of adult KTR outcomes, the prevalence of new-onset diabetes after transplant (NODAT) ranged from 6–15% within one year of kidney transplantation [52]. NODAT risk is higher in those who are older, receiving higher dosages and longer duration of immunosuppressive therapy, and those with concomitant risk factors such as obesity and hypercholesterolemia [53]. Interventions that lower the risk of developing NODAT after kidney transplantation are needed given the adverse effects of hyperglycemia on kidney function over time.

Low glycemic index foods are characterized as carbohydrate-containing foods that lead to lower and delayed elevations in blood sugar (compared to pure glucose), such as whole grains, legumes, and generally unprocessed or lightly cooked foods. Meat, poultry, fish, and eggs do not contain carbohydrates and thus have no glycemic index. In children who are overweight or obese, a meta-analysis of low glycemic index diets suggested that there was an association between reduced insulin resistance and lower triglyceride levels [54]. An intervention prioritizing low glycemic index foods was designed for adult KTRs [55], but outcomes have not yet been published, and there are no studies of such dietary interventions in children with KTRs.

The Mediterranean diet models the dietary patterns of the Mediterranean region and encourages high consumption of fruits, vegetables, legumes, whole grains, nuts, and fish, with olive oil as the main source of fat. It also advises reducing daily consumption of dairy and meat products [56]. The Mediterranean diet has been linked to reduced fasting glucose and rates of diabetes after kidney transplantation in adults [57, 58]. Among adult KTRs, stricter adherence to the Mediterranean diet was associated with lower risk of graft failure, graft loss, and kidney function decline [56]. The effects of the Mediterranean diet in pediatric KTRs have not been studied. A systematic review found that adherence to the Mediterranean diet was poor in children and adolescents, even for those living in Mediterranean countries [59]. Therefore, future research may need to examine the feasibility of implementing the Mediterranean Diet in pediatric KTRs. A summary of dietary interventions that may be useful in pediatric KTRs is provided in Table 3.

Lifestyle interventions targeting dyslipidemia

The prevalence of dyslipidemia increases with increasing transplant vintage, such that over 50% of adults with a history of transplantation during childhood have elevated cholesterol levels [60]. The use of mTOR inhibitors in particular is strongly associated with onset of dyslipidemia. The guidelines from Kidney Disease: Improving Global Outcomes and the AHA recommend annual screening of cholesterol and provision of counseling on therapeutic lifestyle changes as first-line treatments for pediatric KTRs before statin use, as detailed in Table 1 [10, 14].

In a retrospective observational study of 26 pediatric KTRs in Canada, 6 children with hypercholesterolemia who began taking omega-3 fatty acid supplementation for a median duration of 2.5 years (range 0.8–5.9 years) were observed to have lower total cholesterol and triglyceride levels [17]. Although the study recommended specific supplemental doses of the two major long-chain fatty acids (eicosapentaenoic acid, EPA; docosahexaenoic acid, DHA), encouraging regular consumption of omega-3 fatty acid-rich foods (e.g., fish and olive oil) may also be an effective means of increasing omega-3 intake. A recent cross-sectional study of pediatric KTRs in Norway also found that EPA levels were inversely associated with cardiovascular risk factors including triglyceride levels and BP, which supports the consideration of omega-3 fatty acids as an intervention that could potentially mitigate CVD risk in this population [61].

An observational study of 42 pediatric KTRs in Chile found that adherence to an AHA Step II Diet (an intensified version of the AHA Step I diet which recommends taking in < 7% of calories from saturated fat, ≤ 30% of total calories from fat, 10% of calories from polyunsaturated fat, and < 200 mg/day cholesterol intake [62]) was associated with lower total cholesterol and low-density lipoprotein levels [63]. However, there was no observed change in triglyceride, high-density lipoprotein cholesterol levels, or BMI. As discussed earlier, plant-based diets may be associated with meaningful reduction in CVD risk, particularly as it relates to dyslipidemia (see Table 2), although such diets have not specifically been studied in children with KTRs [36].

Conclusion and future directions

Although kidney transplantation ameliorates some of the cardiovascular risk and mortality associated with kidney failure, CVD remains the leading cause of death among pediatric KTRs. The etiology of this persistently elevated CVD risk is multifactorial, but many components that contribute to future CVD are potentially modifiable with lifestyle interventions. Guidelines regarding lifestyle modification interventions to attenuate CVD risk among pediatric KTRs are lacking, but we have highlighted the existing guidelines for lifestyle modification for children. Targeted recommendations for lifestyle modification to improve CVD risk factors among pediatric KTRs are summarized in Table 2.

Diets that have been tested to improve cardiometabolic risk parameters for children and adult KTRs, which may be applicable to pediatric KTRs, are outlined in Table 3. Common dietary elements that we have reviewed include lowering sodium intake; increasing fruit, vegetable, and whole grain intake; and reducing sugar-sweetened beverage intake. Many of the diets described share common features, and further studies are needed to identify customized diets that are feasible for the entire family to adopt and appropriate for pediatric KTRs. Frequent dietitian evaluation and follow-up, when possible, should complement dietary interventions. In addition to dietary counseling, participation in school-based and extracurricular physical activities and at least 5 h of moderate to vigorous physical activity per week should be encouraged in pediatric KTRs. Although we provide general guidelines and data that could be applicable to many pediatric KTRs, an individualized approach considering each child's CKD stage, growth potential and trajectory, functional limitations, and pre-transplantation CVD risk would be prudent.

Lifestyle interventions may be associated with improved CVD risk parameters but can be challenging to implement due to resource intensity, low patient adherence, feasibility, and cost. Adherence is of particular importance among adolescents, who are at the highest risk of graft loss [64]. Pediatric KTRs with chronic rejection and worsening allograft function represent an important subpopulation who would benefit from lifestyle modification, as returning to dialysis would potentially increase the burden of CVD. Many interventions for pediatric patients rely on frequent follow-up, which may not be equitably accessible to all families, particularly those with limited transportation or those living further from a transplant center. Addressing social determinants of health may be important when implementing lifestyle interventions to ensure their success. Creative solutions utilizing technology and telehealth should be explored.

As life expectancy for pediatric KTRs continues to increase, early promotion and development of habits that promote life-long wellness are important to reduce CVD risk. More clinical trials are needed to study the effectiveness of diet and exercise counseling interventions in the pediatric KTR population.

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Key Summary Points

- A majority of pediatric kidney transplant recipients will continue to have one or more cardiometabolic risk factors in the first year after transplantation. CVD remains the leading cause of death in this population.
- Pediatric KTRs should engage in ≥ 5 h of at least moderate-intensity exercise per week and, if pedometers are accessible, set daily step count goals of 15,000 for boys and 12,000 for girls.
- DASH diet, Mediterranean diet, low glycemic index foods, AHA Step II diet, vegetarian or plant-based diets, and low-sodium diets, although not directly tested in the pediatric KTR population, may be useful in lowering BP and weight and improving insulin resistance and cholesterol levels.
- Incentivizing therapeutic lifestyle interventions with rewards, capitalizing on school-based physical activity, and/or gamifying physical activity, as well as ensuring feasibility and accessibility of resources may help improve adherence to lifestyle changes in children.

Multiple choice questions (answers given following the references)

1. Which of the following is *not* associated with an increased risk for new-onset diabetes after transplant (NODAT)?
   - **a.** High dosage of corticosteroids
   - **b.** Younger age
   - **c.** Obesity
   - **d.** Tacrolimus use
2. Which of the following foods is *not* consistent with the Dietary Approaches to Stop Hypertension (DASH) diet?
   - **a.** 4–5 servings of fruits per day
   - **b.** 4–5 servings of vegetables per day
   - **c.** 2–3 servings of dairy per day
   - **d.** > 8 oz of red meat per day
3. Which of the following is recommended by the American Heart Association for children with high-risk health conditions, including kidney transplant recipients?
   - **a.** At least 5 h of physical activity weekly
   - **b.** More than 8 servings of fruits and vegetables daily
   - **c.** Less than 180 min of screen time daily
   - **d.** At least two servings of red meat daily
4. Therapeutic lifestyle changes that may be associated with benefit on cardiometabolic parameters among pediatric kidney transplant recipients include:
   - **a.** Reducing sugar-sweetened beverage intake
   - **b.** Reducing sodium intake to < 2.3 g daily
   - **c.** Increasing full-fat dairy intake
   - **d.** A and B
   - **e.** All of the above
5. Which of the following is a reasonable first step for lowering cholesterol levels in pediatric kidney transplant recipients?
   - **a.** Switching from tacrolimus to sirolimus
   - **b.** Blood pressure reduction
   - **c.** Starting a statin empirically, regardless of the age of the patient

d. Increasing consumption of plant-based foods

Answers to questions: 1. b; 2. d; 3. a; 4. d; 5. d.

Table 1

Comparison of guidelines for cardiovascular risk management in adult and pediatric kidney transplant recipients

	Goal in adult guidelines	Applied to adult KTRs?	Goal in pediatric guidelines	Applied to pediatric KTRs?
Blood pressure	BP < 130/80 mmHg	Yes [9]	< 90^{th} percentile for age, sex, and height < 75^{th} percentile for nonpro-teinuric CKD < 50^{th} percentile for proteinuric CKD	Yes [10, 11] CKD-specific [12]
Physical activity	≥ 150 min/week of at least moderate-intensity physical activity	Yes [9, 13]	≥ 5 h/week of at least moderate-intensity physical activity for high-risk conditions	Yes [10]
Body mass index	< 30 kg/m^2	Yes [11]	< 90^{th} percentile for high-risk conditions	Yes [11]
Sodium intake	< 2000 mg/d in adults with CKD	Not specifically [9]	< 2300 mg/d for children with hypertension	Not specifically [10]
Cholesterol	LDL < 100 mg/dL (2.59 mmol/L); Non-HDL < 130 mg/dL (3.36 mmol/L)	Yes [8, 14, 15]	LDL < 100 mg/dL (2.59 mmol/L)	Yes [4, 10]
Omega-3 fatty acid intake	2000–4000 mg/d of EPA and DHA	Not specifically [16]	Increase intake of EPA and DHA	Yes [17]

KTRs kidney transplant recipients, *BP* blood pressure, *CKD* chronic kidney disease, *LDL* low-density lipoprotein, *HDL* high-density lipoprotein, *EPA* eicosapentaenoic acid, *DHA* docosahexaenoic acid

Table 2

Targeted recommendations for lifestyle modification and potential interventions to improve each cardiovascular risk factor among pediatric kidney transplant recipients

Cardiovascular risk factor	Recommendations and potential interventions
Hypertension	• DASH diet • Sodium intake < 2300 mg/day • AHA diet
Obesity and physical inactivity	• ≥ 5 h/week of at least moderate-intensity physical activity • Setting a daily step-count goal: based on age and sex • BMI < 90th percentile • Incentivize physical activity, integrate games • Ensure exercise interventions are feasible (at home, video-based) • Encourage children to participate in extracurricular physical activities at school
Insulin resistance	• Low glycemic index foods • Mediterranean diet
Dyslipidemia	• Annual evaluation for dyslipidemia • Omega-3 fatty acid supplementation • AHA Step II diet • Vegetarian or plant-based diet

DASH Dietary Approaches to Stop Hypertension, *AHA* American Heart Association, *BMI* body mass index

Table 3

Comparison of diets potentially beneficial for pediatric kidney transplant recipients to reduce cardiovascular disease risk

	DASH	American Heart Association	Mediterranean	Low glycemic index	Vegetarian or plant-based
Main risk factors targeted by the diet	Hypertension	Dyslipidemia	Elevated BMI/weight	Elevated triglycerides, insulin resistance	Elevated cholesterol, insulin resistance
Added benefit of	Decreased total cholesterol	Decrease BP, improved insulin resistance	Elevated HDL	Increased fiber intake	Decreased acidosis, decreased phosphate load, increased fiber intake
Studied in children	Yes [29]	Yes [36]	Yes [59]	Yes [54]	Yes [36]
Studied in pediatric KTRs	No	Yes [63]	No	No	No
Studied in adult KTRs	Yes [27]	No	Yes [57, 58]	No	No

DASH Dietary Approaches to Stop Hypertension, *BMI* body mass index, *BP* blood pressure, *HDL* high-density lipoprotein, *KTRs* kidney transplant recipients