Nutrition in Kidney Disease: Core Curriculum 2022

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As chronic kidney disease (CKD) progresses, the requirements and utilization of different nutrients change substantially. These changes are accompanied by multiple nutritional and metabolic abnormalities that are observed in the continuum of kidney disease. To provide optimal care to patients with CKD, it is essential to have an understanding of the applicable nutritional principles: methods to assess nutritional status, establish patient-specific dietary needs, and prevent or treat potential or ongoing nutritional deficiencies and derangements. This installment of *AJKD*'s Core Curriculum in Nephrology provides current information on these issues for the practicing clinician and allied health care workers and features basic, practical information on epidemiology, assessment, etiology, and prevention and management of nutritional considerations in patients with kidney disease. Specific emphasis is made on dietary intake and recommendations for dietary patterns, and macro- and micronutrients. In addition, special conditions such as acute kidney injury and approaches to obesity treatment are reviewed.

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Am J Kidney Dis. 79(3):437-449. Published online December 1, 2021.

doi: 10.1053/j.ajkd.2021.05.024

The Core Curriculum aims to give trainees in nephrology a strong knowledge base in core topics in the specialty by providing an overview of the topic and citing key references, including the foundational literature that led to current clinical approaches.

Introduction

As chronic kidney disease (CKD) progresses, the requirements and utilization of different nutrients change substantially. These changes are accompanied by multiple nutritional and metabolic abnormalities that are observed in the continuum of kidney disease. To provide optimal care to patients with CKD, an understanding of the applicable nutritional principles and the methods for assessing nutritional status, establishing patient-specific dietary needs, and preventing or treating potential or ongoing nutritional deficiencies and derangements is essential. This installment of *AJKD*'s Core Curriculum in Nephrology provides current information on these issues for the practicing clinician and allied health care workers, with basic, practical information on epidemiology, assessment, etiology, and prevention and management of nutritional considerations in patients with kidney disease. Specific emphasis is made on dietary intake and recommendations for dietary patterns, and macro- and micronutrients. In addition, special conditions such as acute kidney injury (AKI), and approaches to obesity treatment, are discussed separately.

Epidemiology

Individuals with CKD are at risk for a spectrum of nutritional disorders that encompass undernutrition, protein-energy wasting (PEW), and electrolyte disturbances. They also face other challenges such as obesity, secondary prevention of cardiovascular disease, and maintenance of a high-quality diet within the constraints of reduced glomerular filtration (Fig 1). Undernutrition includes protein-energy malnutrition and micronutrient deficiencies. Protein-energy malnutrition, which is caused by inadequate protein and energy intake, results in loss of muscle and fat which, if severe enough, can lead to increased frailty, susceptibility to illness, and even premature death. Undernutrition is different from PEW because the loss of muscle and fat may be due to a variety of causes such as illness, inflammation, acidosis, and insulin resistance, in addition to inadequate nutrient intake.

Correctly diagnosing PEW is challenging because the suggested criteria are extensive and not always easily assessed in clinical settings. Studies suggest the worldwide prevalence ranges from 11% to 54% in persons with CKD stages 3-5 and is between 28% and 54% in patients requiring dialysis. The global prevalence of protein-energy malnutrition in persons with CKD is difficult to estimate because it varies by region and country and lacks a single diagnostic test that is highly accurate, reproducible, and easy to perform in the clinical setting. Hence, the diagnosis is usually based on a combination of history and clinical examination.

There is some evidence that patients with CKD are at risk for micronutrient (vitamins, trace elements, electrolytes) deficiency as a result of possible inadequate dietary consumption, reduced absorption, adherence to dietary prescriptions that may limit micronutrient-rich foods, and dialysis

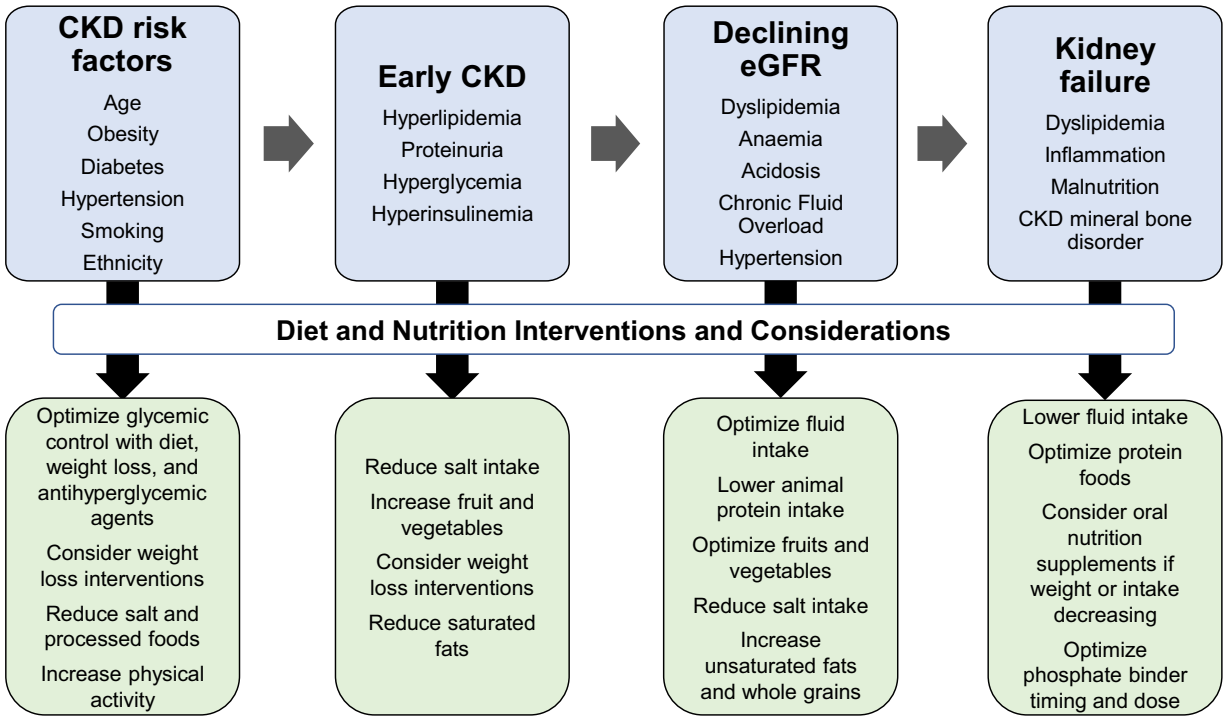

Figure 1. Chronic kidney disease spectrum with nutritional disorders and nutritional interventions considered to be important during each identified phase. Abbreviations: CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate.

procedures that contribute to micronutrient loss. These factors may be compounded by certain illnesses or the use of specific medications. However, the lack of high-quality evidence in this field and the almost complete absence of such studies in patients with CKD who are not on dialysis make it very difficult to determine the true prevalence of individual micronutrient deficiencies.

Overnutrition, which encompasses the other end of the malnutrition spectrum, includes obesity and (rarely) toxicity from excess micronutrient intake. Though protein-energy malnutrition has historically been the major macronutrient derangement in patients with uremia and kidney failure, obesity is arguably now more common in all stages of CKD, at least in the United States. Obesity is important as a major risk factor for the development and progression of CKD and AKI and as an impediment to optimal care of patients with CKD. Obesity in the CKD population clearly shows a rising trend. In 2011-2014 over 44% of persons with CKD stages 3-5 in the United States had obesity, with half of such individuals having severe obesity (ie, body mass index [BMI] > 35 kg/m^2). This represented a 5 percentage point rise over the prior decade. Similar upward trends can be seen in kidney transplant recipients and patients initiating dialysis. Such trends are likely to continue at least into the near future as the prevalence of obesity in the overall population continues to rise.

Assessment of Nutrition Stores

Case 1: *Ms P is a 62-year-old woman regularly attending a CKD clinic, with an estimated glomerular filtration rate (eGFR) of 14 mL/min/1.73 m^2. Her weight, 95 kg, has been stable over the last 2 months, ranging from 92 to 94 kg. Upon examination, you note that she is short of breath and has bilateral ankle edema. She says she has been eating less than usual and is less active due to weakness and fatigue.*

Question 1: Which of the following is the gold standard for body composition assessment in this patient?

a) Anthropometrics and subjective global assessment (SGA)
b) Dual-energy x-ray absorptiometry (DEXA)
c) Bioelectrical impedance analysis (BIA)
d) Magnetic resonance imaging (MRI)

For the answer to this question, see the following text.

The metabolic changes that occur with declining kidney function often result in altered appetite and changes in food intake. Over time this results in loss of nutritional reserves, which are the body stores of muscle and fat tissue. Uremia and the associated inflammation, altered hormones, metabolic acidosis, and changes in gut motility can lead to reduced dietary intake as CKD progresses. Taste changes, poor appetite, and reduced or restricted nutritional intake result in fat and lean tissue loss, which if coupled with volume expansion and edema may remain undetected. Therefore, monitoring body weight alone is not a sufficient means of assessing changes in nutritional stores.

Body weight may remain stable in a state of negative energy balance or undernutrition if edema develops contemporaneously. In dialysis, PEW can be common, and the catabolic state, often due to a combination of reduced intake and inflammation, leads to loss of muscle and fat tissue. The 2012 consensus statement from the Academy of Nutrition and Dietetics and the American Society of Enteral and Parenteral Nutrition recommends that a diagnosis of malnutrition requires that 2 or more of the following are identified: insufficient energy intake, weight loss, loss of muscle mass, loss of fat mass, fluid accumulation (which may mask weight loss), and diminished functional status. Assessment of all these characteristics—including assessment of nutritional stores including muscle mass, body fat, and fluid accumulation—is part of the comprehensive nutrition assessment undertaken in patients with CKD. At the simplest level, nutritional status is likely compromised if there is unintentional weight loss or fluid accumulation together with reduced food intake.

Muscle wasting and subcutaneous fat mass loss can be identified at specific anatomical sites using a physical examination, as in all forms of SGA of nutrition status. Nephrologists, dietitians, nutrition assistants, and nurses can all undertake the SGA as part of routine care, and many dietitians are trained to do so. Specifically, muscle loss at the temples (temporalis), clavicle (pectoralis, trapezius, and deltoids), shoulder (deltoid), scapula (deltoids, trapezius, infraspinatus, latissimus dorsi), between the thumb and forefinger (interosseous), leg (quadriceps), and lower leg (gastrocnemius) can be identified by prominence of bone or hollowing, both identifying loss of muscle tissue. Depletion of fat stores can easily be detected under the eyes (orbital fat pads) and in the upper arms (triceps and biceps skinfold). Fluid accumulation in the extremities or as ascites can mask body mass loss if assessed by weight alone. If edema free weight is not assessed regularly in individuals undergoing dialysis, a reduction in muscle and fat stores may remain undetected until the resulting fluid accumulation is identified clinically.

Handgrip strength measured using a calibrated grip dynamometer serially in an individual can detect a decrease in physical function. Serum albumin, prealbumin, or BMI are no longer considered useful as single markers of nutritional status. Methods requiring specialist equipment and/or significant training and accreditation in technique, such as assessment of body fat by DEXA or skinfold measurements, are not usually available for routine use. DEXA is considered suitable for assessment of fat mass in clinical populations. DEXA is a valid technique for measuring body composition in adult patients with CKD, including post-transplant patients. Although DEXA is also influenced by hydration status in maintenance hemodialysis (HD) and peritoneal dialysis (PD) patients, it is considered as the gold standard. Therefore, the correct answer to question 1 is (b).

Additional Readings

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Etiology and Implications of Nutritional and Metabolic Derangements in Kidney Disease

Case 2: *A 74-year-old woman with history of CKD secondary to diabetes is visiting her nephrologist with concerns of anorexia, nausea, and occasional vomiting. During her evaluation, it is noted that her serum creatinine has risen compared with her most recent (6 months prior) levels, from 2.5 mg/dL to 3.6 mg/dL (eGFR 19 and 12 mL/min/1.73 m^2, respectively). She has been mostly at home with limited activity since her husband died 6 months ago.*

Question 2: Which problem(s) may best explain her recent nutrition and functional decline?

a) Advanced CKD-uremia
b) Depression
c) Decreased physical activity
d) All of the above

For the answer to the question, see the following text.

Multiple factors affect nutritional and metabolic status in patients with moderate to advanced kidney disease, and this can lead to adverse consequences. Accordingly, prevention and treatment strategies should involve an integrated approach to reduce nutrient depletion along with

Table 1. Dietary and Metabolic Changes With Uremic Wasting and Symptoms That Can Respond to Nutritional Therapy

Cause	Mechanism	Complications Amenable to Nutrition Interventions
Reduced intake	Poor appetite (uremic toxicity, inflammation); spontaneous decline in protein intake	Anorexia, nausea, dry mouth, dyspnea
Restrictive dietary intake	Unmonitored restriction of protein and other nutrients	Hypokalemia, unintentional weight loss
Inflammation	Protein catabolism, suppressed albumin synthesis, increased REE	Unintentional weight loss, muscle wasting
GI function	Delayed gastric emptying, impaired motility	Gastroparesis, constipation
Metabolic acidosis	Proteolysis, catabolism of branched-chain amino acids, suppression of albumin synthesis	Hyperkalemia, taste changes
Abnormal hormone response	Altered CHO and lipid metabolism; insulin resistance	Hyperglycemia, hyperlipidemia

Abbreviations: CHO, carbohydrate; GI, gastrointestinal; REE, resting energy expenditure.

interventions that would avoid further losses and replenish already wasted stores. Table 1 displays the dietary and metabolic changes occurring in progressive CKD, their mechanisms, and the resulting symptoms, which may be addressed with nutritional interventions.

A frequent and important cause of PEW in patients with advanced kidney disease is dietary protein and energy intake that is inadequate compared to their needs, primarily due to "uremic" anorexia. The spontaneous and progressive decrease in dietary protein and energy intake seen in CKD patients not yet on kidney replacement therapy usually improves once maintenance dialysis is commenced or a patient undergoes kidney transplantation. Nevertheless, a substantial portion of patients on maintenance dialysis may still have anorexia due to inadequate dialysis and retention of uremic toxins, intercurrent illnesses, chronic systemic inflammation, or depression. Some of the dietary restrictions implemented before initiation of maintenance dialysis are often continued to prevent excessive accumulation of electrolytes such as sodium, potassium, and phosphate, although this practice as a preventative measure is no longer encouraged. Maintenance dialysis is also considered to be a catabolic procedure requiring increased energy intake relative to needs for CKD patients not yet on kidney replacement therapy.

Provision of an adequate dialysis dose to remove uremic toxins is considered a key measure for preventing and treating PEW in maintenance dialysis patients, and a minimum dose of dialysis has been recommended to avoid uremic anorexia and maintain adequate dietary nutrient intake. Data from randomized controlled trials of HD patients (HEMO study) and PD patients (ADEMEX Trial) suggest that what various guidelines consider adequate dialysis is sufficient to maintain nutritional status, although the HEMO study showed that over time patients lose weight regardless of whether they receive an "adequate" dialysis dose. Raising the dialysis dose above the targets determined in these trials has not been shown to improve the nutritional status any further. The results of the Frequent Hemodialysis Network Trial found no meaningful difference in nutritional markers when in-center HD patients were randomized to 6 times per week compared with those receiving the standard 3 times per week.

Nutrient losses through HD membranes (6-8 g per HD session), loss of residual kidney function, increased systemic inflammation from indwelling catheters, use of bioincompatible HD membranes, and PD dialysis solutions can also cause an overly catabolic milieu and increase the minimal amount of nutrient intake required to preserve a neutral nitrogen balance and hence acceptable nutritional stores. Patients who are unable to compensate for this increased need will fall into a state of semistarvation, leading to the development or worsening of PEW.

Systemic inflammation is a major contributor to wasting in patients with advanced kidney disease. Increased systemic levels of inflammatory cytokines such as interleukin 1 (IL-1), interleukin 6 (IL-6), and tumor necrosis factor α (TNF-α) are critical in causing exaggerated protein and energy catabolism, leading to sarcopenia and frailty in chronic disease states. Beyond causing greater protein breakdown, the chronic inflammatory state is associated with lessened physical activity and impaired anabolic actions of insulin and growth hormone; it may also be linked to anorexia on account of its effects on the central nervous system.

In patients with advanced CKD, metabolic acidosis is associated with increased muscle protein catabolism and promotes PEW. Several studies have found improved nutritional status in CKD patients who are given oral bicarbonate supplementation. Based on recent epidemiologic data showing adverse outcomes with high levels of serum bicarbonate before a dialysis session, a target of 24-26 mmol/L is required for patients to avoid metabolic alkalosis after HD. There is evidence that loss of muscle mass in patients with advanced CKD is related to 2 key endocrine abnormalities, namely resistance to insulin and to the growth hormone–insulin-like growth factor 1 (IGF-1) axis. Enhanced protein catabolism occurs in insulin-deficient and insulin-resistant states alike. Patients with advanced CKD also often have other metabolic and hormone disorders (elevated parathyroid hormone concentration, low levels of testosterone, or abnormalities in the thyroid hormone profile), which may also boost hypermetabolism and lower anabolism, leading to excess protein and energy catabolism.

Other comorbid diseases are common in CKD patients and may worsen their nutritional status. In addition to the well-established role of diabetes, CKD patients are also likely

to be protein depleted on account of gastrointestinal disturbances (eg, diabetic gastroparesis, nausea and vomiting, pancreatic insufficiency, or bacterial overgrowth and impaired protein absorption in the gut). Polypharmacy makes these gastrointestinal complications worse. The answer to question 2 is therefore (d), all of the above.

Additional Readings

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Nutritional Management of Patients With Kidney Disease

In the last decade there has been a paradigm shift in the nutritional management of CKD. The focus has moved away from management of specific nutrients and toward the broader perspective of whole diets and dietary patterns. Observational studies suggest that dietary patterns that promote cardiovascular health, such as diets based on eating vegetables, nuts, legumes, whole grains, and fish and poultry, with less red meat and fewer processed foods, are associated with reduced mortality and reduced risk of CKD progression. Evidence from a small number of clinical trials of dietary patterns or nutritional interventions that address the whole diet have demonstrated the beneficial effects of whole-diet interventions for slowing kidney function decline in stage 3-4 CKD and improving protein and energy intake in patients receiving HD and improving the lipid profile in kidney transplant recipients.

Medical Nutrition Therapy

Case 3: *Ms B is a 56-year-old woman with CKD secondary to diabetes. Her eGFR is 19 mL/min/1.73 m², and her diabetes is poorly controlled. Her blood work indicates a random blood glucose of 162 mg/dL (9 mmol/L), serum potassium of 5.8 mEq/L (5.8 mmol/L), and serum bicarbonate of 18 mEq/L (18 mmol/L).*

Question 3: What factor(s) would you address to treat the hyperkalemia?

a) Reduce fruit and vegetables.
b) Correct the acidosis.
c) Treat the hyperglycemia.
d) b and c. If hyperkalemia is not resolved, then review her whole diet.

For the answer to the question, see the following text.

Medical nutrition therapy in CKD aims to meet nutritional requirements for food groups, macronutrients, and fiber while reducing the risk of hyperkalemia and hyperphosphatemia. Achieving the balance between adequate and varied nutritional intake and safety is achievable with the skills of a dietitian to educate patients and provide individualized recommendations based on a detailed holistic assessment. Dietitians are also skilled in addressing barriers to improving nutritional intake; they can help improve energy and protein intakes via behavior change approaches. Providing generic advice focused on safety without also ensuring access to a dietitian may increase the likelihood of patients adopting overly restrictive diets with resulting inadequate nutrition.

Dietary patterns are rapidly becoming a major focus of medical nutrition therapy in CKD. Encouraging certain dietary patterns is a sharp contrast with the restrictive dietary approaches that have dominated nutrition interventions for decades. The guidelines now suggest that specific nutrient restriction is not needed unless serum levels are elevated unsafely. Therefore, a more individualized approach is encouraged, and dietitians experienced in managing CKD can expand dietary choices for fruit, vegetables, nuts, legumes, and whole grains in a stepwise manner when serum levels permit. Furthermore, adopting a dietary pattern approach enables providers who do not have specific nutrition expertise to provide holistic dietary recommendations to their patients with CKD.

Nutritional therapy in early CKD should focus on high fruit and vegetable intakes for their beneficial effects on blood pressure, blood lipids, acid-base balance, and their fiber content. With mild to moderate reductions in eGFR, a diet high in fruit and vegetables, with moderate amounts of dairy foods and meat and poultry, may be beneficial due to several mechanisms. In studies by Goraya et al (2013) comparing high fruit and vegetable intake to sodium bicarbonate and to control conditions, the fruit and vegetable intake was as effective as sodium bicarbonate for reducing acidosis and slowing the decline in eGFR without increasing serum potassium, and it was superior to sodium bicarbonate for decreasing body weight, systolic blood pressure, and low-density lipoprotein (LDL) cholesterol. Overall, when intake of fruit and vegetables was increased by 2 cups per day, it led to a lower acid load and higher dietary fiber, which may be protective against hyperkalemia due to faster bowel transit time and have favorable effects on gut microbiota.

The Mediterranean diet pattern—which is high in fruits, vegetables, legumes, whole grains, nuts, and olive oil, with moderate amounts of poultry and seafood, and contains little red meat, sweets, or processed foods—can improve the lipid profile of kidney transplant patients and may be beneficial in CKD to slow down the onset of kidney failure. Dietary patterns based on fresh foods and whole grains are naturally lower in salt and absorbable phosphates, so they have beneficial effects for blood

Table 2. Nutrition Interventions in CKD When Individualized Medical Nutrition Therapy Is Not Available

Nutritional Consideration	Rationale	Examples of Interventions
Maintaining health and minimizing risks from comorbid conditions (eg, diabetes, CVD, hypertension, obesity)	Dietary pattern impacts on disease risk more than individual nutrients or foods. Lower salt intake reduces risk factors.	• Cook from fresh ingredients when possible. • Include vegetables and whole grains with meals every day. • Choose legumes or plant-based meat alternatives, reduce meat portions, and limit processed meats. • Personalize meal plans to meet energy needs.
Addressing barriers to changing eating behaviors	Food choices are multifactorial.	• Individualize strategies for addressing identified barriers. • Use behavioral therapy techniques such as self-monitoring and self-directed goal setting.
Hyperkalemia	Consider all possible causes before reducing high nutritional value fruits and vegetables. Use fruit and vegetables to reduce net acid load and provide dietary fiber.	• Stage 1: Address possible nondietary causes such as hyperglycemia, acidosis, constipation, recent medication changes, or use of potassium-sparing diuretics. • Stage 2 (if required): Reduce lower-nutritional value foods such as potato chips, fruit juices, and chocolate. • Stage 3: Peel, chop, and boil vegetables, access pictorial or color-coded resources for lower-potassium-containing fruits and vegetables, and maintain recommended number of servings per day.
Hyperphosphatemia	Consider food additives, protein requirements, and dialysis adequacy.	• Limit processed meats, processed cheese, and processed cheese products. • Choose fresh meat, poultry, or fish without added phosphates (read food labels). • Legumes, soy products, nuts, and whole grains have lower phosphate availability as they contain nondigestible phytates. • Ensure phosphate binder doses are matched to mealtimes and protein/phosphorus intake.
Optimizing nutritional status	Reduce mortality risk, and improve quality of life.	• Personalize meal plans to meet energy needs. • May need supplemental nutrition when fatigue is limiting factor or intake is poor.

Abbreviation: CKD, chronic kidney disease; CVD, cardiovascular disease.

pressure and serum phosphate levels. Dietary education can encourage patients with CKD to consume a healthy diet by favoring home cooking and reducing the intake of processed and convenience foods.

Table 2 lists the major considerations for nutrition interventions in CKD and some examples of how more generalized interventions may be delivered in CKD when medical nutrition therapy is not available. Specific, tailored medical nutrition therapy is implemented by dietitians, who follow a holistic assessment to derive a nutritional diagnosis and consider multiple factors that impact food-related behaviors.

As eGFR declines and hyperkalemia develops, there are several potential contributing factors to consider. Hyperglycemia and metabolic acidosis can cause potassium to shift extracellularly. Correction of acidosis with sodium bicarbonate or treatment of hyperglycemia with insulin can restore equilibrium and allow the potassium to shift back into cells. Thus, the best answer to question 3 is (d). If serum potassium is elevated with normal acid-base balance and euglycemia, dietary modifications to reduce potassium intake from lower nutritional value foods is recommended after other nondietary causes such as medications are considered and addressed, if medically appropriate to do so. Meat, fish, and dairy foods often contribute more dietary potassium than fruits and vegetables, so consideration of the dietary pattern or a whole-diet plan is required for optimal management. It is important to note that dietary modifications are now recommended only to treat hyperkalemia and not as a preventative measure. When possible, individuals with CKD should be encouraged to eat a variety of plant foods for dietary fiber, cardioprotection, and the beneficial effect on gut microbiome.

Additional Readings

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Dietary Nutrient Intake

Protein Intake

Case 4: *Mr Y is a 65-year-old man with CKD secondary to hypertension. His eGFR is 24 mL/min/1.73 m². He is very adherent to office visits and medications.*

Question 4: Which of the following is the recommended level of dietary protein intake for this patient?

a) 0.28-0.43 g/kg body weight per day
b) 0.55-0.60 g/kg body weight per day
c) 0.80-0.90 g/kg body weight per day
d) 1.00-1.20 g/kg body weight per day

For the answer to the question, see the following text.

The rationale for reducing dietary protein intake in CKD is that a lower protein load reduces hyperfiltration and lowers the production of uremic toxins, including p-cresyl sulfate, indoxyl sulfate, trimethyl aminoxide, and fibroblast growth factor 23 (FGF-23). Protein intake recommendations in stages 3-5 CKD, without diabetes, range from 0.55 to 0.6 g/kg per day to reduce the risk of kidney failure or death (odds ratio, 0.621 [95% CI, 0.391-0.985]), although a reduction in protein intake to 0.55-0.6 g/kg per day had no clear effect on decline in eGFR. However, another review comparing normal protein intakes of 0.8 to >1.0g/kg per day to protein intakes of 0.5-0.6 g/kg per day in stage 3 CKD found little or no difference in rates of death or kidney failure. For those with diabetes, protein intakes of 0.6-0.8 g/kg per day are recommended. Both animal and plant protein sources can be encouraged, with no nutritional advantage of animal protein over plant-based sources. Protein intake of 0.55-0.6 g/kg per day is only sustainable in a stable, neutral metabolic state and should only be undertaken under close clinical supervision with the intent to reduce clinical symptoms and delay initiation of dialysis. Protein intakes of 0.55-0.6 g/kg per day are not recommended during hospitalization, during infection or treatment with immunosuppressive medications, or during or after short-term loss of body weight. Furthermore, whether actual body weight, ideal body weight, or adjusted body weight is used to calculate protein may be determined using clinical judgement and personalized to individuals.

Beyond examining protein restriction alone, several studies have looked at the effects of keto acid– or amino acid–supplemented low-protein diets (LPDs) or very-low-protein diets (VLPDs) on certain metabolic and kidney outcome parameters. Because the supplemental keto acids are primarily given to substitute for dietary protein intake, most of these studies are with VLPDs. Accordingly, several meta-analyses indicate that VLPDs supplemented with keto acids delay the initiation of maintenance dialysis and significantly reduce urea production, along with having potentially beneficial effects on insulin resistance and oxidative stress. From a safety perspective, well-designed diets planned by skilled dietitians and implemented by motivated and adherent patients are effective and do not harm the nutritional condition. The recommended level for VLPD is 0.28-0.43 g dietary protein per kilogram of body weight per day with additional keto acid/amino acid analogs to meet protein requirements (0.55-0.60 g/kg per day).

In HD and PD, there is an absence of randomized controlled trials for protein intake and outcomes. Based on observational studies, the recommended protein intake is 1.0-1.2 g/kg per day when in a stable metabolic state and with adequate energy intake. With diabetes, higher protein intake may be required to achieve glycemic control. Therefore, the correct answer to question 4 is (b).

Energy Intake

To maintain normal nutritional status, the 2020 KDOQI nutrition guideline recommends prescribing an energy intake of 25-35 kcal per kilogram of body weight per day based on age, sex, physical activity level, body composition, weight status goals, CKD stage, and concurrent illness or presence of inflammation. These considerations are required when estimating energy requirements for individuals because they determine overall energy balance. The ratio of carbohydrate, fat, and protein for individuals with CKD depends on CKD stage and coexisting comorbidities such as diabetes, cardiovascular disease, and obesity. Generally, carbohydrates make up around 50% of energy intake, with the remainder from protein and fat.

Carbohydrate Intake

When protein intake is limited, such as when using a low-protein diet to prevent the buildup of uremic toxins, carbohydrate intake will need to increase to meet energy requirements. Carbohydrates include starches and sugars, with a preference for starchy foods that are less processed such as whole grains, including brown rice, whole wheat bread or pasta, oats, barley, and spelt. Whole grain carbohydrate sources contain more B vitamins and dietary fiber than refined carbohydrates. Fiber is important for reducing gut transit time, which reduces intestinal potassium absorption and reduces cholesterol, decreasing gut toxins and supporting a healthy gut microbiota. Whole grain foods are now encouraged in CKD because in less refined starches the phosphorus is present as phytate, which is not digestible in the human gut and so does not contribute to dietary phosphorus.

Potatoes and other starchy vegetables are often dietary staples and can be included in the diets of those with CKD.

Potatoes, sweet potatoes, and yams all contain potassium, which can be reduced in cooking by cutting the tubers into small pieces then soaking and boiling them in water before eating or by further cooking via roasting or baking or mashing. Cutting, soaking, and heating destroys some of the cellular structure, releasing the potassium from the food.

Naturally occurring sugars in fruit, vegetables, milk, and plain yogurt do not contribute to the health risks associated with free sugars, so they can be eaten in moderation as part of a healthy diet with CKD. The free sugars found in soda, cordials, sugar-sweetened beverages, cookies, and cakes are associated with heart disease and becoming overweight or obese, and they have low nutritional value. These types of sugars should be avoided unless overall energy intake is poor.

Fat Intake

CKD patients commonly have dyslipidemia, with abnormalities in lipid profiles detectable as kidney function starts to decline. Nephrotic syndrome or other comorbid conditions such as diabetes mellitus and liver disease as well as the use of drugs that affect lipid metabolism (eg, thiazide diuretics, β-blockers) contribute further to the dyslipidemia evident in this population.

In patients receiving maintenance HD, increased serum triglycerides and very-low-density lipoproteins and decreased LDL and high-density lipoproteins (HDL) are the most common abnormalities. The elevation in triglycerides is believed to be linked to elevated levels of apolipoprotein CIII (Apo-CIII), which inhibits lipoprotein lipase. Increased lipoprotein (a) (Lp[a]) levels are also seen in a substantial percentage of maintenance HD patients. Patients treated with PD have higher levels of serum cholesterol, triglyceride, LDL cholesterol, and Apo-B than those seen in patients on maintenance HD, even though the mechanisms altering lipid metabolism are shared between the 2 groups. This may be due to increased protein losses through the peritoneum, perhaps by mechanisms related to the nephrotic syndrome, and by the glucose load of the dialysate leading to higher triglyceride synthesis and hyperinsulinemia. PD patients also have higher levels of Lp(a).

The dietary management of dyslipidemia in the setting of kidney disease is not well-established, except in kidney transplantation. In general, CKD patients are recommended to follow the general advice for heart health, including saturated fat less than 7% of total energy and unsaturated fat, such as olive oil, to substitute for saturated fats including butter and animal fats.

Micronutrient Intake

Micronutrients include vitamins, trace elements, and electrolytes and are essential for optimal biological function. The main concern in patients with CKD is that as a result of reduced dietary intake or dietary restrictions, comorbid conditions, and/or losses through the dialysis procedure deficiencies in certain vitamins and trace elements may develop. However, excess intake of certain micronutrients may also occur, leading to vitamin toxicity (eg, vitamin C, vitamin D) or clinical complications (eg, sodium, potassium, phosphorus). Because the delicate balance between underconsumption and overconsumption is also influenced by the stage of CKD and each person's unique needs and risk factors, developing an optimal dietary strategy in persons with CKD can be challenging.

Vitamins. Studies have suggested that patients with CKD are at risk for deficiencies in vitamin B_1 (thiamine), B_2 (riboflavin), and B_3 (niacin), vitamin C, vitamin K, and vitamin D. However, the studies were nearly all performed in persons on maintenance dialysis and from varying geographic regions and time periods, making it difficult to apply these conclusions to individual patients. Moreover, dietary reference intakes for individual vitamins (and other micronutrients) are not available for the CKD population as they are in the general population.

Due to concern beginning decades ago over possible micronutrient deficiencies, particularly with water-soluble B vitamins, vitamin supplements tailored to patients with CKD were developed. Presently 70% of maintenance HD patients in the United States are prescribed such supplements. Yet the evidence for routine supplementation is thin. A reasonable alternative strategy would be to supplement only those individuals who by history or examination exhibit impaired dietary intake and/or nutrient loss for sustained periods of time.

Electrolytes. Although electrolyte intake in patients with CKD should always be tailored to individual needs, a few general suggestions can be offered. Sodium consumption should be limited to less than 100 mmol/d (2.3 g) to help control blood pressure and limit extracellular volume expansion. Replacing bread, processed meats, and cheese with fresh meats, fish, brown rice, legumes, and whole wheat pasta can reduce sodium intake. Because major sources of dietary potassium are fruits, vegetables, legumes, and nuts, all of which contain high levels of fiber and other micronutrients that offer potential health benefits, efforts should be made to avoid automatically restricting these foods unless the individual's serum potassium is elevated and other nondietary causes of hyperkalemia have been considered and addressed.

Similarly, the consumption of fruits and vegetables, which contain natural alkali, should be encouraged if possible because they can help reduce the complications of kidney disease–related systemic acidosis such as bone damage, muscle loss, and a possible decline in residual kidney function. Dietary phosphorus intake should be adjusted to maintain serum phosphorus levels in the normal range. Phosphorus should ideally be obtained

from plant-based foods, such as whole grains, legumes, and pulses, because the phosphorus is typically less well absorbed and whole grain foods have a higher nutritional value compared with processed foods that contain phosphate additives.

The intake of dietary calcium in patients with CKD stages 3-4 should be to achieve 800 to 1,000 mg daily to maintain a neutral calcium balance. The intake goals in more advanced disease may be complicated by concurrent use of vitamin D analogs and calcimimetics.

Trace Elements. Information on trace elements such as zinc, selenium, or a number of other metals found in minute concentrations in the body in persons with CKD is sparse. Therefore, routine supplementation of trace elements is not recommended.

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Nutritional Supplementation

Case 5: *A 74-year-old woman who has had type 2 diabetes mellitus and has been on maintenance HD for 5 months is noted to have had a gradual weight loss from premorbid 68 kg to the current 59 kg. For the last 3 months, she has had problems with eating. She states that she does not tolerate meals well (usually less than half consumed), and she had a very poor appetite. She especially feels weak the afternoons after dialysis and has had no energy to cook a full meal on those days. Her dialysis time is at 11:00 AM, which interferes with her lunch. She was offered nutritional supplements, which she has tried to drink once in the morning and once at supper. She has had trouble tolerating supplements due to fullness and some bloating.*

Question 5: Which step(s) would you take to address her signs and symptoms of early satiety, gastrointestinal disturbances, fatigue, weight loss, and reduced nutritional intake?

a) Review her medications, the adequacy of her dialysis, and her acid-base balance.
b) Request (or complete) a nutritional assessment (eg, SGA) of her body stores, gastrointestinal symptoms, functional capacity, and food intake to determine factors contributing to her poor nutritional state.
c) Review the timing and type of her nutritional supplement (or request a dietitian to review the timing and type of her nutritional supplement).
d) All of the above.

For the answer to the question, see the following text.

When intake from food alone is inadequate, supplementation with nutrition formulations can be used to meet nutritional requirements to prevent or treat malnutrition. In CKD, undernutrition is associated with poorer outcomes, and using nutritional interventions is warranted in these patients. Oral nutritional supplements (ONS), enteral tube feeding, and parenteral nutrition may be used when clinically indicated (Box 1). In reference to case 5, all the options are appropriate and should be completed to provide the most suitable nutritional care of the patient. Thus, the best answer to question 5 is (d).

ONS are suitable when oral intake is possible and safe. Enteral tube feeding using a nasogastric tube or gastrostomy tube is suitable when it is unsafe to swallow or when adequate nutrition cannot be consumed orally. Box 2 provides a list of several important considerations when prescribing oral nutritional supplementation.

Box 1. General Indications for Supplemental Feeding, Enteral and Parenteral Nutrition with Chronic Kidney Disease

Oral Supplementation

If any one of the following indications are present:
- Eating < 75% of usual meals for > 7 days with acute illness
- Weight loss of 5% in 1 month with acute illness
- Mild to moderate loss of subcutaneous fat stores or muscle mass
- Eating < 75% of usual meals for at least 1 month with coexisting chronic illness
- Weight loss of 7.5% in 1 month with coexisting chronic illness
- Compromised swallow requiring modified texture diet ± thickened fluids

Enteral Tube Feeding
- When unsafe to swallow
- When adequate nutrition cannot be consumed orally

Parenteral Nutrition
- When digestive tract is inaccessible or nonfunctioning
- Intradialytic supplemental parenteral nutrition may be used during hemodialysis when specific criteria are met if oral nutrition supplementation has been unsuccessful

Box 2. Factors to Consider When Prescribing Oral Nutritional Supplements (ONS)

- To maximize benefit, prescribe ONS 2 to 3 times daily (preferably 1 hour after meals) rather than as a meal replacement.
- Total protein and energy intake may be increased with provision of a monitored high-protein meals or ONS service during maintenance hemodialysis.
- Consider patient taste and texture preferences when ONS is prescribed.
- Tolerability of ONS should also be carefully monitored as some patients may develop gastrointestinal symptoms with ONS.
- Energy-dense and low-electrolyte, kidney-specific ONS may be considered when fluid overload and electrolyte derangements are evident.

If there is no requirement for fluid restriction or electrolyte modification, standard ONS and enteral feeds may be used with ongoing monitoring. Special considerations with CKD include providing adequate energy and protein within a reduced volume as well as electrolyte modification, depending on the eGFR and serum electrolyte levels. If fluid restrictions and/or electrolyte modification is required, nutrient-dense, lower-volume, or kidney-specific products should be considered. In many cases, a high-energy oral nutrition supplement or enteral nutrition formula with fiber is an appropriate first-line choice.

Parenteral nutrition is used when the digestive tract is inaccessible or nonfunctioning, and it is usually managed by a multidisciplinary team. Intradialytic parenteral nutrition (IDPN) is a form of supplemental nutrition support that may be useful in a narrow therapeutic range. By definition, it is parenteral nutrition supplied during HD and can therefore be given only as often as dialysis. Generally, IDPN can assist to meet nutritional requirements if patients are achieving 20 kcal/kg per day but are unable to meet their full energy requirements. The frequency of usage of IDPN in the United States has not been reported but it is likely to be uncommon. Nephrologists typically order the IDPN, sometimes with expert support from the company providing the IDPN. Financial barriers may exist because the estimated cost of IDPN is ~$300 per day compared with a few dollars for oral supplements. Many insurers cover IDPN only if specific eligibility criteria are fulfilled (including failure to respond to oral or enteral nutrition). IDPN therapy has a potential for complications that include electrolyte and lipid disorders.

Dietary Supplements

Dietary supplements used to prevent or treat disease, also known as nutraceuticals, are quite popular in the general populace and have also been studied to some extent in patients with CKD. For example, fish oil–derived long chain omega-3 polyunsaturated fatty acids (eicosapentaenoic acid [EPA], docosahexaenoic [DHA]) are known to mediate cell membrane physiology, eicosanoid production, signal transduction, and the inflammatory cascade. Several modestly sized studies in patients on maintenance HD found no benefit of fish oil supplementation on sudden cardiac death, cardiovascular disease, or HD access thromboses. However, it does lower triglyceride and LDL levels and raise HDL levels. Antioxidant therapy in the forms of vitamin E, coenzyme Q, acetylcysteine, bardoxalone methyl, or human recombinant superoxide dismutase has not been shown to improve cardiovascular outcomes or overall mortality, but better powered studies are needed to confirm these results.

Pharmacological Interventions

Anabolic Hormones

Men receiving maintenance HD very commonly have testosterone deficiency, which is associated with increased mortality risk and decreased muscle function. A number of clinical trials showed significant benefits for HD patients with nandrolone decanoate treatment in terms of anthropometric (eg, body weight, BMI, skinfold measurements) and biochemical parameters as well as serum concentrations of total protein, prealbumin, and transferrin.

Anti-inflammatory Agents

Given that systemic inflammation causes an exaggerated protein catabolic response, treatment with specific and nonspecific anti-inflammatory agents has been suggested as a novel strategy to prevent the development or worsening of PEW in patients with CKD. The preliminary data using anticytokine therapies and high-dose omega-3 administration are intriguing; however, long-term studies are needed to determine whether there are reproducible effects of anti-inflammatory strategies in patients with advanced CKD.

Appetite Stimulants

In experimental animal studies, ghrelin, a stomach-derived growth hormone–releasing hormone able to stimulate appetite via the central nervous system, has been found to increase muscle mass. There is a long history of using appetite stimulants such as megestrol acetate, melatonin, cyproheptadine, and dronabinol to improve appetite in maintenance dialysis patients, but there has been no systematic examination of their efficacy.

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Acute Kidney Injury

Nutritional requirements in hospitalized patients with AKI are variable and largely depend on the severity of AKI, the setting, the underlying disease process, and the treatment provided. The nutritional hallmark of AKI, especially in the setting of critical illness, is excessive catabolism. Factors that have been postulated as the underlying mechanism for this high rate of protein and energy catabolism include concurrent illnesses leading to exaggerated proinflammatory cytokine release, inability to feed patients because of surgical and other reasons, and metabolic derangements predisposing patients to diminished utilization and incorporation of available nutrients. Whether uremic toxin accumulation further exacerbates these abnormalities is questionable because aggressive dialytic clearance does not substantially improve mortality in stage 3 AKI patients.

The nutritional markers that correlate best with efficacy of nutritional therapy and patient outcomes are considerably different in AKI patients than in CKD patients. Blood levels of biochemical markers such as serum albumin and prealbumin are influenced by volume status and concurrent inflammatory state. Similarly, the use of traditional measures of body composition such as anthropometry has limited application in AKI patients owing to major shifts in body water.

The aim of nutritional care in patients with AKI is to support their nutritional needs safely to minimize further metabolic imbalance. In patients deemed to be noncatabolic, standard nutritional modifications may only be required if there is an identified electrolyte imbalance or modified fluid requirement. The Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines recommend that for critically ill patients the energy requirements be determined using indirect calorimetry or estimated as 25-30 kcal/kg per day with ongoing monitoring and adjustment, as clinically indicated. Protein requirements in these patients range from 1.2 to 2.0 g/kg per day and may increase up to a maximum of 2.5 g/kg per day for those requiring frequent or continuous kidney replacement therapy. In critically ill patients, standard enteral nutrition formulations are appropriate unless significant electrolyte abnormalities are evident, in which case specific nutritional formulations with a modified electrolyte profile may be considered. Provision of large quantities of nutrients, especially intravenously, may result in more fluid administration and predispose patients to fluid overload, resulting in earlier initiation of dialytic support.

Hospitalized Patient With Underlying Kidney Disease

It is important to note that nutritional guidelines for use in CKD apply when the individuals with CKD are otherwise reasonably well and living in the community. The nutritional requirements for hospital patients with CKD as an underlying condition will be modified by the metabolic state and comorbid conditions present in the acute hospitalization period. In situations where patients are in an acute catabolic state, protein and energy intake should be increased to meet acute requirements. Modifications to dietary patterns should occur when the patient is metabolically stable.

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Obesity

The global obesity problem has profound implications for nephrology due to its wide and growing prevalence and its substantial impact on CKD. Obesity is a mediator of kidney disease, predominating through the development of proteinuria, AKI, CKD, and kidney failure. The mechanisms include a variety of direct (intraglomerular shear-related damage, podocyte stress, fat infiltration, lipotoxicity, and upregulated renin-aldosterone and sympathetic systems) and indirect (development of type 2 diabetes, hypertension, and cardiopulmonary disease) causes (Fig 2). Obesity also impedes optimal care of patients with CKD by, for example, precluding many obese patients from undergoing kidney transplantation

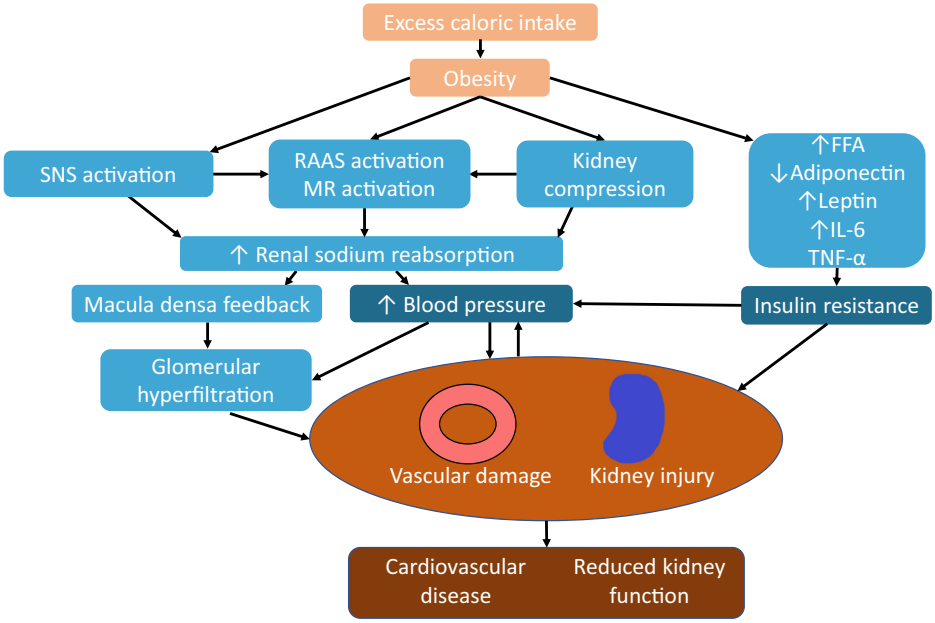

Figure 2. The interplay between obesity, hypertension, kidney injury, and cardiovascular disease. Abbreviations: FFA, free fatty acid; IL-6, interleukin 6; MR, mineralocorticoid receptor; RAAS, renin-angiotensin-aldosterone system; SNS, sympathetic nervous system; TNF-α, tumor necrosis factor α. Based on information in MacLaughlin, 2013 (*Weight Loss Interventions in Obese Patients With Chronic Kidney Disease,* [doctoral thesis, King's College London]) and Hall et al, 2019 (*Nat Rev Nephrol.* https://doi.org/10.1038/s41581-019-0145-4).

and limiting the success of dialysis access placement and function. Finally, obesity greatly increases the burden of disease and disability in people with CKD.

Treatment options for obesity in patients with CKD include dietary and lifestyle interventions, pharmacotherapy, and bariatric (now also known as metabolic) surgery. Accumulating evidence demonstrates that weight loss may ameliorate or even prevent the development of CKD, though the exact amount of weight loss needed to accrue these benefits and the precise benefits are still being elucidated. In most people with obesity, the body "defends" against weight loss through upregulation of hormonal and other mechanisms. This explains why for the majority of the population weight loss is best achieved and maintained through medications or metabolic surgery that help to reset these mechanisms.

Of the 4 antiobesity drugs approved by the US Food and Drug Administration, only the glucagon-like peptide 1 (GLP-1) agonist liraglutide, which lowers weight by as much as 8 kg on average, can safely be used in all stages of CKD. Newer and even more powerful GLP-1 agonists alone or in combination with other drugs are expected to soon enter the market that may induce an average of 16%-20% or greater weight loss. They would constitute major advances in antiobesity treatments for patients with CKD if found to be safe in that population.

Metabolic surgery offers the largest and most sustained weight reduction of any treatment option. In randomized trials, metabolic surgery showed much greater benefits in improving or remitting major CKD risk factors like type 2 diabetes and hypertension compared with nonsurgical weight loss strategies. A growing body of observational studies has found that metabolic surgery may slow the development and progression of CKD and may even reduce mortality in people with preexisting CKD. Though increasing severity of CKD is associated with more complications after metabolic surgery, even for individuals with advanced CKD the perioperative and mortality risks are only modestly higher than in the general population. Thus, metabolic surgery should be considered safe and effective for patients with CKD. However, no evidence-based guidelines currently exist to help determine which individuals with CKD would most benefit from such surgery.

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Support: None.

Financial Disclosure: Dr MacLaughlin reports consulting fees from Abbott Nutrition and Nestle. Dr Friedman reports consultant fees from GI Dynamics and Goldfinch Bio. Dr Ikizler reports personal fees from Fresenius Kabi, Abbott Renal Care, and Nestle.

Peer Review: Received January 14, 2021, in response to an invitation from the journal. Evaluated by 2 external peer reviewers and a member of the Feature Advisory Board, with direct editorial input from the Feature Editor and a Deputy Editor. Accepted in revised form May 21, 2021.