

The Case for a Bariatric-Centered Approach to Chronic Kidney Disease Care

Allon N. Friedman

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Not too long ago, nephrologists were mainly interested in nutrition to understand how uremic cachexia and resultant protein-calorie undernutrition influenced their patients' wellbeing. How times have changed. As the prevalence of obesity skyrockets to over 650 million individuals worldwide, the opposite of protein-calorie undernutrition—obesity—has now taken its place front and center as the main nutritional and metabolic disorder in persons with CKD.

The rapid rise in obesity and its adverse consequences have converged like sledgehammers on the kidneys of our patients. Unfortunately, overwhelmed by the number and complexity of their patient load, nephrologists are neither inclined to dip their toes in the obesity management pool nor trained to recognize it as a problem within their purview. This is unfortunate because obesity is the source of some of the most common and serious risk factors for CKD. Integrating obesity management or at minimum improving awareness of this issue in standard nephrology practice in a more concerted, proactive, and consistent manner is therefore likely to reap important benefits for our patients and greater society.

Obesity Is Highly Pervasive in the CKD Population

Between 2011 and 2014 nearly half of individuals with CKD in the United States were obese while one quarter were severely obese (1). This reflects an increase across all levels of severity of obesity over the past 15 years. Although more recent data are not available there is no reason to expect that this trend has leveled off.

Obesity Is a Linchpin for CKD Risk Factors

Type 2 diabetes mellitus and hypertension are well established complications of obesity and are also the first and second most common causes of incident ESKD in the United States. Obesity independently predicts the development of proteinuria and ESKD in individuals with and without CKD. Obesity can cause a form of FSGS and is linked to a decline in kidney function in glomerular diseases like IgA nephropathy and inherited diseases like polycystic kidney disease. Finally, obesity increases the risk for nephrolithiasis, kidney cancer, and AKI. Although up

to 30% of CKD cases in the United States have been attributed to being overweight or obese (2), the true figure is invariably higher when one includes the impact of obesity-related diabetes and hypertension. Thus CKD in the modern age is, to a very large degree, a consequence of obesity.

Intentional Weight Reduction and Protection against Kidney Disease

Weight loss strategies includes lifestyle/dietary/pharmacologic (medical) and metabolic (aka bariatric) surgery interventions. There is strong evidence from short- to moderate-term randomized, controlled trials and longer-term observational studies that weight reduction—particularly *via* metabolic surgery, which offers greater and more sustained weight loss—leads to regression or remission of major risk factors for CKD including diabetes, insulin resistance and hyperinsulinemia, hypertension, dyslipidemia, obstructive sleep apnea, and intraglomerular hypertension. Cardiovascular and total mortality risk is also reduced.

Although research into the effect of weight reduction on the development and/or progression of CKD is at a much earlier stage, preliminary evidence suggests that it may offer kidney protection. In terms of medical management, a small proof-of-concept study found that a very low 12-week caloric diet in patients with very advanced proteinuric diabetic kidney disease resulted in large weight loss and led to improvements in a variety of short-term markers of metabolic and kidney disease (3). But such a restrictive diet may not be necessary to achieve kidney protection. A secondary analysis of the Action for Health in Diabetes (Look AHEAD) trial, which randomized 5145 obese patients with type 2 diabetes and mostly normal baseline kidney function to an intensive lifestyle intervention or usual care (4), found that the intervention (which lowered weight an average of 4 kg) was associated with a 31% reduction of developing very-high-risk CKD over an 8-year median follow-up period.

With regard to metabolic surgery, several recent observational studies report that it is associated with improvements in albuminuria, eGFR, and prognostic risk for CKD (5–8). Two of these studies also reported slower progression to a composite end point of ESKD and stage 5 CKD or doubling of serum creatinine (5,7).

Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana

Correspondence:

Dr. Allon N. Friedman, Indiana University School of Medicine, 550 University Boulevard, Suite 6100, Indianapolis, IN 46202. Email: allfried@iu.edu

Especially intriguing are the possible kidney protective benefits in patients with or at risk for diabetic kidney disease (7,9,10).

Yet this body of literature suffers from a number of notable gaps that must be overcome to better define the benefits of weight loss on kidney health. Among these are the lack of data from randomized, controlled trials, the dearth of studies (randomized or otherwise) that include substantial numbers of patients with preexisting CKD, and the lack of statistical power to detect differences in hard outcomes like ESKD, hospitalization, and death. The safety of such interventions in patients with CKD also needs to be better clarified, particularly for bariatric surgery which in addition to standard surgical risks carries with it the potential for kidney-specific problems like AKI and oxalate nephropathy. Determining which patients with CKD are optimal candidates for weight loss interventions is necessary to maximizing the benefit-to-risk ratio and the use of scarce resources. Finally, investigators need to untangle through prospective studies the complex “obesity paradox” phenomenon observed in patients with ESKD, which posits that obesity is beneficial. Fortunately some of these gaps are currently being addressed in ongoing or planned clinical studies.

Nephrologists as Advocates for Weight Loss

The process of involving nephrologists in overseeing or helping manage weight loss in their overweight or obese patients with CKD faces several major challenges. The first involves professional barriers related to time constraints, reimbursement, and the like. The second involves knowledge deficits related to the proper management of obesity. The third involves a lack of awareness of how central a role obesity plays in mediating CKD risk. The last involves the difficulty inherent in effectively treating obesity, regardless of the population.

These are indeed formidable obstacles but the alternative option—ignoring the opportunity to target arguably the major source of CKD risk—does a disservice to our patients, especially because they may not receive much assistance with this issue from their primary care physicians.

Progress on this issue must begin somewhere and nephrologists have much to gain by identifying the problem and taking corrective steps. For many or even most nephrologists, correction might simply mean acknowledging that the problem exists, educating patients on its importance, and referring them to established weight management programs. Successful weight management could potentially achieve in one stroke what nephrologists normally struggle to do in several: improve dysglycemia, control hypertension, downregulate the renin-angiotensin-aldosterone axis, lower sodium avidity in the kidneys, reduce proteinuria, ameliorate pulmonary hypertension, reverse glomerular hyperfiltration, and minimize stone risk. Additional benefits, such as improving eligibility for kidney transplantation and creating better functioning dialysis accesses, may also arise. Finally, if future clinical trials demonstrate that weight reduction slows onset of CKD or progression to ESKD or reduces hospitalization or death rates, this will offer yet another incentive to integrate weight management into nephrology practice.

Strategies to Strengthen Obesity Management in the Field of Nephrology

The process of obesity management will involve nephrologists and their patients and families. Possible steps in this process are:

- Improving education on the biologic basis for obesity as a disease and its effect on risk factors for CKD.
- Becoming familiar with the spectrum of weight management strategies and their risks and benefits in patients with CKD.
- Forming working relationships with local obesity physicians and programs and educating them about the CKD population. Select nephrologists may actually want to consider establishing their own weight management programs tailored specifically for patients with CKD.
- Raising awareness of obesity so that weight management becomes an automatic part of the treatment plan for every patient.
- Avoidance of medications that lead to weight gain and use of medications that induce weight loss.
- Involving patients’ family members in the treatment process.

Various institutional stakeholders will also need to play a role by:

- Encouraging professional education, perhaps by partnering with other professional organizations like The Obesity Society, the American Society for Metabolic and Bariatric Surgery, and the American Diabetes Association.
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None.

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