Advances in Practice

Implications and Treatment Options for Overweight and Obese Patients with Chronic Kidney Disease

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Patients undergoing maintenance dialysis frequently experience malnutrition, which may develop prior to dialysis initiation, resulting in loss of lean tissue and fat stores, and increased morbidity and mortality (1-3). However, several recent studies report a high prevalence of overweight in the dialysis population that parallels the rapid increase in excess body weight in the non-renal population (4-6).

In the United States, 61% of adults are overweight, as indicated by body mass index (BMI) >25 kg/m^2, and the age-adjusted prevalence of obesity (BMI > 30 kg/m^2) increased from 13% to 23% between 1960 and 1994 (7). When years of life lost due to overweight and obesity was estimated using data from the U.S. Life Tables, Third National Health and Nutrition Examination Survey (NHANES III), First National Health and Nutrition Epidemiologic Follow-Up Study (NHANES I and II) and NHANES II Mortality Study, obesity was found to significantly decrease life expectancy (8).

A study of the influence of excess weight on morbidity and mortality in 1346 hemodialysis (HD) patients in Mississippi revealed that 38% of these patients had BMI > 27.5 kg/ m^2 (4). More recently, 38% of patients in a Spanish HD population were found to have BMI $\geq$ 25 kg/m^2 (6). In addition, data from a national transplant database reveals that 60% of subjects undergoing kidney transplantation are overweight or obese (9).

This column will review the influence of excess body weight on health outcomes in patients with chronic kidney disease (CKD), guidelines for appropriate body weight and interventions to promote weight control in this population.

Excess body weight and health outcomes in patients with chronic kidney disease

Although elevated BMI increases risk of cardiovascular disease (CVD) and mortality in the non-renal population, higher BMI has been associated with improved one-year survival rates in patients undergoing maintenance HD therapy (4,5). In addition, an inverse correlation has been demonstrated between adjusted mortality rate and BMI at initiation of maintenance HD (10).

However, when the association between BMI and survival was investigated in a population of non-diabetic renal patients over a 12-year period, mortality was higher in patients with BMI > 19 kg/m^2 (11). The higher mortality in these patients was associated with CVD risk factors, including low levels of high-density lipoprotein (HDL)-cholesterol and elevated total cholesterol to HDL-cholesterol ratio. Thus, this study indicates that high BMI may have a negative impact on long-term survival in patients undergoing maintenance HD.

It is not clear whether higher BMI is associated with better survival in patients undergoing peritoneal dialysis (PD) because different studies have shown conflicting results. Snyder et al investigated body size and outcomes in 418,000 United States Medicare patients initiating PD between 1995 and 2000, and concluded that overweight (BMI 25.0-29.9 kg/ m^2) and obese (BMI >29.9 kg/ m^2) patients survive longer than those with lower BMI (12). However, when data from the Australia and New Zealand Dialysis and Transplant Registry was used in multivariate analysis of outcomes in all new adult patients undergoing PD between 1991 and 2002, obesity (BMI >29.9 kg/ m^2) was independently associated with death and technique failure (13).

More recent findings from a retrospective study of patients in the United States Renal Data System (USRDS) Dialysis Morbidity and Mortality Wave II Study (DMMS) show no survival advantage for PD patients with BMI $\geq$ 30 kg/m^2 compared with those with lower BMI (14).

Obesity has been more strongly linked with increased risk for calciphylaxis, which frequently occurs within the first year after initiating maintenance dialysis therapy (15). This condition leads to calcification of the walls of small blood vessels, resulting in ischemia and necrosis of the skin, subcutaneous fat, visceral organs and skeletal muscle, and causing significant morbidity in the form of pain, infection and organ failure.

In the early stages of CKD, obesity may promote the progression of renal disease (16). Severe obesity is associated with increased blood flow to the kidneys, higher glomerular filtration rates (GFR) and development of glomerulopathy (17). Renal biopsies performed on severely obese adolescents (BMI 46 ± 11 kg/m^2) with unexplained heavy proteinuria (3.1 ± 1.3 g/dL) revealed glomerular hypertrophy and focal glomerulosclerosis (18).

The association between severe obesity and glomerulosclerosis may lie in the increased serum leptin concentrations exhibited by these individuals. Leptin is a hormone produced by the ob gene in adipose tissue and linked with regulation of food intake (19). However, leptin is also a renal growth factor. In animal studies, leptin infusion causes proliferation of glomerular endothelial cells, resulting in glomerulosclerosis and proteinuria (20).

Hypertension, which often accompanies obesity, also contributes to renal dysfunction by increasing glomerular pressure, capillary damage and proteinuria (21). When obese patients lose weight, blood pressure control improves, and GFR and proteinuria are both reduced (17,18,22). In the Trials of Hypertension Prevention, Phase 1, hypertensive men and women ages 30-54 assigned to an 18-month lifestyle modification program for weight loss showed a 77% reduction in risk for

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hypertension after seven years, compared with controls (22).

The influence of obesity on outcomes following renal transplantation has also been studied. Obese patients (pre-transplant BMI $\geq$ 30 kg/m^2) have a significantly higher incidence of delayed graft function and wound infections post-transplant than a matched non-obese control group (pre-transplant BMI < 30 kg/m^2) (23). In addition, obesity is often accompanied by hyperhomocysteinemia after kidney transplantation, which independently increases risk of developing atherosclerosis and CVD (24).

Guidelines for appropriate body weight in patients with chronic kidney disease

While obesity clearly impacts health outcomes in patients with CKD, there is little consensus on what constitutes appropriate body weight for this population. Fleischmann et al concluded that morbidity and mortality might be reduced in HD patients through proper nutrition directed to achieve BMI at the high end of the normal range (20-27.5 kg/m^2) (4). On the basis of epidemiological data, Kopple et al established a goal of maintaining BMI in the upper 50th percentile ($\geq$ 23.6 kg/m2 for men and $\geq$ 24.0 kg/m^2 for women) in adult maintenance dialysis patients (5). In an editorial comment on the relationship between body weight and survival in the dialysis population, Salahudeen recommended that patients maintain a high-normal BMI (25). The recently published Guidelines for Nutrition Care of Renal Patients suggest a goal BMI of 20-25 kg/m^2 for adult dialysis patients (26).

The Kidney Disease Outcomes Quality Initiative (K/DOQI) Clinical Practice Guidelines for Nutrition in Chronic Renal Failure use standard body weight (SBW) to define an appropriate body weight for patients with CKD (27). Based on data from NHANES II, SBW is the 50th percentile for body weight for healthy Americans of the same age range, gender, height and frame size as the patient in question. The guidelines recommend that patients maintain a weight that is 90 - 110% of SBW and that body weight $\geq$ 115% SBW indicates obesity.

Interventions to promote weight control in patients with chronic kidney disease

The K/DOQI Nutrition Clinical Practice Guidelines recommend using edema-free body weight (BWef) to prescribe calories for adult maintenance dialysis patients (27). BWef is the post-dialysis weight for HD patients, and weight after drainage of dialysate in PD patients. The recommended daily calorie intake is 35 kcal/kg for maintenance dialysis patients under the age of 60 years, and 30-35 kcal/kg for those aged 60 or older.

However, for patients with BWef >115% SBW, use of adjusted edema-free body weight (aBWef) is recommended (27):

aBWef = BWef + [(SBW - BWef) x 0.25]

Basing calorie prescription on aBWef in obese dialysis patients takes into account the lower calorie requirements of adipose tissue, compared with lean body mass.

Behavioral weight reduction programs have been implemented successfully to achieve and maintain weight loss in obese HD patients (28). Nevertheless, patients attempting weight reduction face the same obstacles to behavior change as patients trying to adopt a therapeutic diet for chronic disease. These obstacles include problems selecting and preparing foods, poor palatability, lack of support, difficulty in choosing appropriate foods at restaurants and social gatherings, and loss of autonomy (29-33). Renal dietetics professionals can help these patients achieve their weight loss goals by individualizing dietary interventions and providing regular follow-up.

There are no guidelines for managing obesity specifically in nondialyzed patients with CKD and educational materials are not readily available. However, weight reduction is an essential step in controlling hypertension, which is associated with obesity and increases risk for renal diseases (34, 35). In line with National Heart, Lung and Blood Institute (NHLBI) guidelines, a reasonable initial goal for this population is to reduce body weight by approximately 10% from baseline (36).

Two articles from an educational website directed at patients with CKD emphasize gradual weight loss through diet and exercise, and warn against use of amphetamine-like products, prescription medications and herbal supplements (37, 38). However, intervention by a registered dietitian is needed to translate general information on weight control into an individualized eating pattern.

Patients with CKD approaching the need for dialysis, and those already undergoing maintenance dialysis therapy, may be motivated to lose weight in order to increase their eligibility for a renal transplant. Among patients undergoing maintenance dialysis therapy, those with BMI > 28.7 kg/m2 have lower rates of enrollment on the renal transplant waiting list than those with BMI 24.5 - 28.7 kg/m^2 (39). In addition, obese patients gain more weight after transplant surgery than non-obese patients (40).

Intensive post-transplant dietary counseling is necessary to control weight gain in renal transplant recipients. Patel studied thirty-three renal transplant patients receiving similar immunosuppressive therapy who were divided into two groups (41). One group received no dietary advice or follow-up post-transplant. Patients in the other group were advised on diet, exercise and weight control before leaving the hospital; the dietary advice was individualized and follow-up was provided at regular intervals up to four months post-transplant. Dietary information comprised advice on complex carbohydrates, sugar, fiber, fat and protein, and included individualized meal and exercise plans. During follow-up sessions, additional information was provided on shopping, convenience foods, appropriate snacks and strategies for weight maintenance.

Comparison of the two groups at four months post-transplant showed an average weight gain of 1.4 kg in those who received dietary advice, and 7.1 kg in the control group. At one year post-transplant, average weight gain was 5.5 kg in the intervention group and 11.8 kg in the control group. While this study demonstrates that

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dietary advice and follow-up reduce weight gain in renal transplant recipients, it also emphasizes the need for continued follow-up beyond four months post-transplant to manage body weight.

Another approach to the management of severe obesity in renal transplant recipients involves gastric bypass (GBP) surgery. Morbidly obese patients (200-260% of their ideal body weights) who were six to eight years post renal transplant experienced significant weight reduction, and improvements in hypertension and hyperlipidemia, following Roux-en-Y gastric bypass (42). During this procedure, a small stomach pouch is created to restrict food intake. In addition, a Y-shaped section of the small intestine is attached to the pouch, allowing food to bypass the lower stomach, duodenum and first part of the jejunum. By 12 months post GBP, weight loss reached a plateau as patients achieved 100-150% of ideal body weight. GBP has been used to alleviate co-morbid conditions and improve quality of life in obese HD patients with BMI $\geq$ 35 kg/m^2 and awaiting transplant (43). Some of these patients subsequently received a renal transplant.

Vertical banded gastroplasty (VBG) has also been used to promote permanent weight loss and enhance quality of life in the obese transplanted population (44). In VBG, a band and staples are used to create a small pouch in the upper stomach. This restricts food intake and prolongs satiety, without producing malabsorption.

VBG has the advantage over GBP of allowing absorption of nutrients and immunosuppressive medications from the upper gastrointestinal tract, but GBP promotes greater weight loss (43,44). There are no published guidelines for nutritional care of patients with CKD and GBP. However, these patients must be monitored closely to ensure adequate intake of protein, folic acid, vitamin B12, magnesium, iron and calcium (43).

Summary

The renal dietetics professional has early and ongoing contact with patients with CKD, and therefore plays a vital role in implementing lifestyle interventions to optimize health. This member of the renal care team also has the expertise to evaluate nutritional needs and provide individualized dietary advice to promote weight control in this population. Management of obesity in patients with CKD may slow the progression of renal disease, improve long term survival in maintenance dialysis patients, decrease risk of calciphylaxis and increase eligibility for renal transplantation.

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