

Obesity: Growing Impact on CKD

Obesity is a multifaceted problem and has the potential to cause or contribute to metabolic disorders such as diabetes, dyslipidemia, hypertension, and the metabolic syndrome. Recently, obesity has been identified as an independent and major risk factor for chronic kidney disease. Ejerblad et al¹ stated in a recent paper, "Our results confirm an accumulating body of evidence and experimental data implicating obesity as an important causative factor for kidney disease.... For all subtypes, obesity doubled or tripled the risk of chronic renal failure (CRF)." As the prevalence of obesity increases, so shall the cost to individuals and society in increasing morbidity, early mortality, and lost productivity. According to the third annual report of the National Kidney Foundations' Kidney Early Evaluation Program (KEEP),² which summarized health information on 37,155 individuals who are at risk for kidney disease, 77% of participants were classified as obese, and 53% had evidence of chronic kidney disease (CKD). Participants in KEEP must have a personal history of diabetes or hypertension or a family history of diabetes, hypertension or kidney disease.² That the overwhelming majority are overweight or obese highlights the daunting task that lies ahead in preserving the health of persons with multiple risk factors and comorbidities for both cardiovascular and kidney disease.

Ross and McGill³ start this issue with a discussion of the epidemiology of obesity and CKD. Despite the independent association described for obesity and CKD, the major impact of obesity on the kidney is most likely mediated through comorbidities such as hypertension, diabetes, and the metabolic syndrome. Ejerblad and colleagues¹ confirmed that the strongest link between obesity and CKD was for diabetes-related kidney disease. Wang et al⁴ review the available data on obesity in children with CKD and find that obesity appears to hasten the progression and is associated with increased mortality. Faster progression means that renal replacement therapy is needed at younger ages in children who are obese, which further aggravates the disability and mortality risk.

Mechanisms for progression are explored in the article by Chalmers et al⁵ in an article that discusses the many fluid, electrolyte, hemodynamic, and metabolic perturbations found in obesity that may contribute to more rapid progression of CKD. One such problem is the metabolic syndrome, which shares many features with typical CKD patients: abdominal obesity, hypertension, abnormal lipid parameters, and mild or worse glucose disposal.⁵ Insulin resistance, along with many other disturbances in the renin-angiotensin system, fibrinolytic system inflammation, and adipocyte-derived hormones are shared between obesity and CKD patients, according to Lastra et al.⁶

Insights are often gained from the study of appropriate animal models for the disease in question. Mak et al⁷ focus on mouse models for obesity that have led to the discovery of leptin, the leptin receptor, and the role of sterol regulatory element-binding proteins in diet-induced obesity. Mice that are naturally resistant to the development of nephropathy can be coaxed into it by high-fat feeding, which highlights the importance of diet as the sentinel event in obesity-related kidney disease.

Medicine becomes less about making diagnoses and understanding the details of pathogenesis, molecular abnormalities, and genetic aberrations of disease when a patient is present in the room and needs assistance with real-life problems. Solving the problem of obesity involves an understanding of behavior and mechanisms of behavior change. Doyle et al⁸ probe the process of change, with a focus on adolescent patients with obesity. This group of challenging patients faces change on multiple fronts that they cannot always control, but need to take charge of their health by modifying many different behaviors, including dietary choices. Understanding the process of choice is necessary for those who hope to assist with behavior change. Anderson and

Miller⁹ discuss the nutrition recommendations for persons with obesity and CKD and point out the difficulties of conflicting dietary advice for those in need of weight reduction while dealing with reduced excretory capacity. Doctors and caretakers should try to find palatable nutrition while following these guidelines for a week or so. Empathy and practical expertise will increase in the process. For patients with morbid obesity and medical comorbidities, questions about bariatric surgery often arise. Despite the limited data available on the topic, Zalesin and McCullough¹⁰ provide a thorough review that discusses the risks and benefits of bariatric surgery for the CKD patient. Bariatric surgery may become an earlier option for patients who are unsuccessful at losing weight and who face medical morbidity as an ongoing consequence of their obesity.

Miller¹¹ tackled the subject of planning for renal-replacement therapy in patients with obesity. Interestingly, after facing increased morbidity and mortality with CKD, obese patients may have a survival advantage in the early stages of end-stage renal disease (ESRD). Whether one type of replacement is significantly better than others remains to be determined; however, obesity adds another set of problems to already complex patients.

In summary, the problem of obesity is growing and will result in more patients with CKD of all ages facing health hazards of unseen proportions. The potential to have an impact on the progression of kidney disease by assigning higher priority to obesity as a risk factor cannot be overstated. An estimated 650,000 people will require dialysis treatment by 2010.¹² Substantial public-health and economic benefits will result from attenuating the rising incidence of end-stage kidney disease, given the overall annual mortality of 20% and Medicare expenditures of \$25 billion yearly. Worldwide, obesity will worsen IgA, urate nephropathy, and many other types of kidney disease and will result in early mortality. Public-health and prevention strategies that begin before birth, extend through childhood, and

continue in adulthood are needed to maintain a healthy populace.

Janet B. McGill, MD
Washington University, St. Louis, MO

Susan Furth, MD, PhD
Johns Hopkins University, Baltimore, MD

Frederick J. Kaskel, MD
*Albert Einstein School of Medicine,
New York, NY*

References

1. Ejerbad E, Fored CM, Lindblad P, et al: Obesity and risk for chronic renal failure. *J Am Soc Nephrol* 17: 1695-1792, 2006
2. Kidney Early Evaluation Program: KEEP annual data report, 2005. *Am J Kidney Dis* 46:1-158, 2006 (suppl 3)
3. Ross WF, McGill JB. Epidemiology of obesity and chronic kidney disease. *Adv Chronic Kidney Dis* 13: 325-335, 2006
4. Wang Y, Chen WW, Klag MJ, et al: Epidemic of childhood obesity: Implications for kidney disease. *Adv Chronic Kidney Dis* 13:336-351, 2006
5. Chalmers L, Kaskel FJ, Bamgbola P: The role of obesity and its bioclinical correlates in the progression of chronic kidney disease. *Adv Chronic Kidney Dis* 13: 352-364, 2006
6. Lastra G, Mannrique C, Sowers JR: Obesity, cardiometabolic syndrome and chronic kidney disease: The weight of the evidence. *Adv Chronic Kidney Dis* 13:365-373, 2006
7. Mak RH, Kuo HJ, Cheung WW: Animal models of obesity-associated chronic kidney disease. *Adv Chronic Kidney Dis* 13:374-385, 2006
8. Doyle M, Siegel R, Supe K: Stages of change and transitioning for adolescent patients with obesity and hypertension. *Adv Chronic Kidney Dis* 13:386-393, 2006
9. Anderson CA, Miller ER: Dietary recommendations for obese patients with chronic kidney disease. *Adv Chronic Kidney Dis* 13:394-402, 2006
10. Zalesin KC, McCullough PA: Bariatric surgery for morbid obesity: Risks and benefits in chronic kidney disease. *Adv Chronic Kidney Dis* 13:403-417, 2006
11. Miller BW: Planning for renal replacement therapy in the patient with obesity. *Adv Chronic Kidney Dis* 13:418-420, 2006
12. Xue JL, Ma JZ, Louis TA, et al : Forecast of the number of patients with end-stage renal disease in the United States to the year 2010. *J Am Soc Nephrol* 12:2753-2758, 2001