Assessment and management of chronic kidney disease in people living with obesity

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Obesity and chronic kidney disease (CKD) are common and frequently coexisting medical conditions. Already well known to be a risk factor for type 2 diabetes mellitus (T2DM), ischaemic heart disease, stroke, hypertension, malignancy and premature death, obesity also predisposes to CKD. Elevated weight leads to declining renal function through several mechanisms, including established pathways via metabolic syndrome, hypertension and T2DM, but also through relatively recently understood glomerulosclerosis, directly related to obesity. Compared with non-obese comparators, people living with obesity and established CKD develop faster decline in glomerular filtration, progression to end-stage renal disease (ESRD) and death. Importantly, treatment of obesity can influence these crucial renal outcomes and significantly improve quality of life. Declining renal function also impacts the medical and surgical treatment options available to treat patients with overweight and obesity. In this article, we briefly outline the epidemiology of obesity and renal disease and review the pathological interactions between these diseases before focusing on considerations for assessment and evidence-based treatments for obesity and renal disease.

KEYWORDS: obesity, chronic kidney disease

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Obesity and CKD epidemiology

In 2022, 25.3% of adults over 18 years of age in the UK were living with obesity and a further 37.9% had overweight but not obesity according to body mass index (BMI) criteria. In the same year, 3.98% of adults were diagnosed with chronic kidney disease (CKD) in the UK Quality and Outcomes Framework (QoF) data. Both of these figures are expected to grow in the coming years and, given the high cost and quality of life implications of end-stage renal disease (ESRD), represent a serious public health concern.

Assessment

There are no clear guidelines related to the diagnosis and assessment of CKD within people with obesity. Measurement of creatinine or urinary protein or albumin does not form part of the work-up for obesity as recommended by the National Institute for Health and Care Excellence (NICE) CG189 Obesity: Identification, Assessment and Management Clinical Guideline. Fortunately, renal function is a readily available and commonly performed blood test and forms a standard part of the assessment of many other obesity-related complications, including type 2 diabetes mellitus (T2DM), hypertension and cardiovascular disease.
Severe obesity is associated with poorer performance of standard eGFR. Use of alternative methods, such as CKD-EPI, might provide a higher performance, particularly in people with GFR <60 mL/min per 1.73 m².18

Ascribing the cause of declining renal function definitively to obesity or one of its complications can be challenging. ORG is typically associated with a subnephrotic range proteinuria, which might be a helpful diagnostic tool in the absence of diabetes or hypertension. As in other conditions exhibiting hyperfiltration, proteinuria can be observed before a demonstrable decline in eGFR. Renal biopsy is rarely indicated because it is unlikely to influence management and is technically more challenging in patients with obesity, though ORG can be definitively diagnosed histopathologically if other causes of renal disease are suspected.

Among people with established renal failure, assessment of weight is crucial and complete nutritional assessment should occur twice annually in patients with CKD stage 3–5.19 Helping people to lose weight is not only helpful in reducing the risk of cardiovascular disease, but can also help improve renal specific outcomes, thus avoiding ESRD.

### Management of weight in people with impaired renal function

Weight loss in people with overweight and obesity has significant positive effects on a range of features. With specific focus on renal disease with eGFR >30 mL/min per 1.73 m², weight loss has been associated with improvements in microalbuminuria, overt proteinuria and hyperfiltration, and can completely reverse renal dysfunction.20 Multiple meta-analyses of weight loss in CKD have been conducted with a clear benefit of weight loss on important renal outcomes.20,21 Regression analyses within one of the meta-analyses demonstrated that, for each 1 kg weight loss, there was a 110 mg reduction in proteinuria and a 1.1 mg reduction in albuminuria, which is independent of weight loss method and improvements in hypertension.20

In people with eGFR <30 mL/min per 1.73 m², malnutrition, reduced lean body mass and sarcopenia are more prevalent and weight loss might worsen outcomes. A higher BMI has been associated with improved outcomes in some studies and, therefore, weight loss interventions in this group should be individualised and considered only with specialist support and guidance.

### Physical activity and calorie restriction

People with coexisting overweight and obesity as well as CKD should be supported to achieve physical activity levels in line with the general population. In the UK, the Chief Medical Officer’s Physical Activity Guidelines encourage adults to accumulate 150 min of moderate intensity activity or 75 min of vigorous intensity activity per week. Periods of prolonged sedentary activity should be minimised as much as possible and broken up with at least light activity on a frequent basis.22

Physical activity and caloric restriction leading to modest improvements in weight have been demonstrated to improve markers of inflammation and stress in people with moderate to severe CKD.

A complex assessment of dietary recommendations in ESRD is beyond the scope of this article. In ESRD, a ‘Mediterranean diet’ is recommended to aid lipid metabolism and weight loss.19

There is little evidence to support the use of very low-calorie (600–800 kcal/day) meal replacement diets for weight loss in people with severe and complex obesity in ESRD and might be difficult to administer in patients with ESRD on dialysis. These approaches can be considered on an individualised basis with support of obesity and renal specialist clinicians and dieticians. Further high-intensity dietary interventions have been trialled successfully in the dialysis population, but it remains unclear whether these high-intensity interventions are feasible outside the context of a clinical trial.21

### Pharmacological therapies

Orlistat is a gastrointestinal tract lipase inhibitor that decreases dietary fat absorption and forms part of the NICE guidance for obesity in conjunction with diet, exercise and behavioural modification. It is associated with modest weight loss but its use is limited by the high prevalence of gastrointestinal side effects resulting from its mechanism of action. The British National Formulary recommends caution with orlistat in CKD and there are no specific studies evaluating its efficacy or safety in ESRD; however, a single non-randomised clinical trial in people with obesity and CKD stage 2 and a GFR of 60–90 mL/min demonstrated safety and efficacy in weight loss in conjunction with an intervention including education, an exercise program and a low-fat diet.24 There are rare case reports of orlistat-induced oxalate nephropathy further limiting its use.25

Metformin, an oral biguanide, is the first-line treatment for T2DM. In combination with diet and exercise, metformin can contribute to a modest weight loss of 1–5 kg in people with T2DM, but is not effective in people with normal glucose metabolism.26 This modest weight loss, a side effect of appetite reduction, is important given its widespread use; however, it is insufficient as monotherapy for individuals with obesity. Metformin use can lead rarely to lactic acidosis in patients with advanced CKD particularly in the context of sepsis; therefore, guidelines recommend dose lowering with progressive renal dysfunction and cessation once CKD stage 4 with a GFR of <30 mL/min is established.

Glucagon-like peptide-1 (GLP-1) is an incretin hormone with wide-ranging effects, including enhancement of glucose-dependent insulin secretion, inhibition of glucagon secretion, delayed gastric emptying and increased satiety. Injectable GLP-1 receptor agonists (GLP-1RAs) have been available for many years; however, novel long-acting weekly preparations have demonstrated cardiovascular benefits and significant weight loss and have become a mainstay of treatment for obesity. Improvements in hard renal outcomes (reduced incidence of new or worsening CKD) were observed in participants with coexisting T2DM treated with a once-weekly GLP-1RA.27 In people without T2DM treated with GLP-1RA, renal benefits have not yet been demonstrated, although improvements in cardiovascular outcomes merit their use.28 Given the tolerability at very low eGFR, these drugs are likely to feature prominently in weight loss management strategies in people with CKD with or without T2DM in the future. GLP-1RAs can also be used for weight loss in the run up to renal transplantation (including for people on dialysis) and are safe to continue after transplantation.29

Sodium-glucose cotransporter 2 inhibitors (SGLT2i) lower blood glucose through reduced tubular reabsorption of filtered glucose. SGLT2i are effective at reducing progression of renal failure in people with and without diabetes30,31 independent of their
glycosuric effects. SGLT2i are associated with a small amount of weight loss in CKD (1 kg) and cannot be considered a mainstay of weight loss management despite their other utilities in this group of patients. Numerous novel agents are being developed to enhance weight loss. One of these, a dual GLP and gastric-inhibitory peptide agonist, has demonstrated impressive improvements in weight loss, but has also demonstrated reduced decline in renal function and might be a helpful tool when it becomes commercially available in the UK.

**Complications of peritoneal dialysis in people living with obesity**

Obesity has been associated with worse outcomes from peritoneal dialysis (PD). One study identified an increase in death rates on PD with increasing weight. Although this has not been replicated recently, there are reports of more frequent complications, such as peritonitis, again leading to increased healthcare utilisation.

**References**