Diabetic nephropathy: changes after diabetes surgery?

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Abstract

Introduction: Obesity, as a central piece inside metabolic syndrome, is associated with early chronic kidney disease (CKD). In addition, several observational, cross sectional, and longitudinal studies have demonstrated that obesity is an independent risk factor for the onset, aggravated course, and poor outcomes of CKD including diabetic nephropathy. This implies that when obesity is reversed, many CKD risk factors and CKD itself could be favorably influenced. So all measures aimed at weight loss are recommended to minimize risks from obesity-related conditions and generate improvements in the metabolic profile. Recent evidence shows that bariatric surgery (BS) can revert or improve proteinuria and CKD in morbidly obese patients.

Objectives and methods: The present review is aimed to provide the evidence regarding the beneficial effects of weight loss after BS in different stages of CKD including kidney transplant recipients, with a special focus on the beneficial effect in reducing or improving proteinuria and renal failure. Furthermore, this updated systematic review of the literature analyzes potential adverse effects that BS could induce not only on renal function but also on morbidity and mortality risk in perioperative and postoperative period.

Conclusions: Results from the different case reports, meta analysis as well as systematic review of clinical trials show that obesity treatment by way of lifestyle changes, pharmacotherapies and BS can reduce proteinuria and help to prevent loss of renal function. Also BS may reduce complications, and allow obese patients with end-stage renal disease to undergo kidney transplantation with good results.

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Key words: Obesity. Chronic kidney disease. Microalbuminuria. Proteinuria. Weight loss.

Resumen

Introducción: La obesidad, como pieza clave dentro del síndrome metabólico, está asociada con el enfermedad renal crónica (ERC) temprana. Además, varios estudios observacionales, de corte transversal y longitudinal han demostrado que la obesidad es un factor de riesgo independiente para la aparición, progresión y empobrecimiento del pronóstico de la ERC incluida la nefropatía diabética. Esto implica que cuando se revierte la obesidad, mejora mucho de los factores de riesgo de ERC y la propia ERC. Por lo tanto, todas las medidas encaminadas a la pérdida de peso permitiría minimizar los riesgos asociados a la obesidad y mejorar el perfil metabólico. La evidencia actual ha demostrado que la cirugía bariátrica (CB) puede revertir o mejorar la proteinuria y la ERC en pacientes con obesidad morbida.

Objetivos y métodos: Esta revisión tiene como objetivo proporcionar evidencia sobre los efectos beneficiosos de la pérdida de peso tras la CB en los diferentes estadios de la ERC incluido los receptores de trasplante renal, especialmente los efectos beneficiosos en la reducción o mejora de la proteinuria y de la insuficiencia renal. Además, esta revisión sistemática actualizada de la literatura analiza los efectos adversos potenciales que podría producir la CB no solo sobre la función renal, sino también sobre la morbimortalidad en el período peri y postoperatorio.

Conclusiones: Los resultados de los diferentes casos clínicos, metaanálisis, así como, revisiones sistemáticas de los ensayos clínicos demuestran que el tratamiento de la obesidad mediante cambios en el estilo de vida, tratamiento farmacológico y CB pueden reducir la proteinuria y prevenir la pérdida de la función renal. Asimismo, la CB minimiza las complicaciones, y permite a los pacientes obesos con ERC avanzada recibir un trasplante renal con buenos resultados.

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Introduction

The epidemic of obesity and type 2 diabetes (T2DM) is on the rise worldwide at an alarming rate. The International Diabetes Federation estimates that in 2003, 194 million people had diabetes, and that by 2025, 333 million people will have this disease. This epidemic is taking place in both developed and developing nations. In the U.S. alone, at least 16 million people have T2DM, with 1 million more being diagnosed annually. Obesity is also increasing at alarming rates. In the U.S., the majority diagnosed with T2DM are overweight, of which 50% are obese (i.e., body mass index (BMI) > 30 kg/m²) and 9% are morbidly obese (BMI > 40 kg/m²). Evidence from several studies indicates that obesity and weight gain are associated with an increased risk of diabetes and that intentional weight loss reduces of developing diabetes. Each year, an estimated 3.000.000 US adults die of causes related to obesity, and diabetes is the sixth leading cause of death. Correspondingly, both obesity and diabetes generate immense health care costs. A substantial portion of the health costs attributed to obesity is related to T2DM. Also T2DM and its complications have substantial socioeconomic impact on the patients, their family and society. It is an inexorably progressive disease, leading to deterioration in multiple organs and systems, and the most common cause of adult blindness, limb amputations, and renal failure in Western communities, as well as the leading independent risk factor for coronary artery disease.

Prevention of diabetes and obesity, through effective public health initiatives to modify the population’s dietary habits and lifestyle should be of highest priority. Lifestyle modifications including behavioral therapy, diet, and exercise aimed at weight loss are recommended to minimize risks from obesity-related conditions and generate improvements in the metabolic profile and quality of life. Unfortunately, dietary and pharmacological therapies are relatively ineffective in achieving or maintaining adequate weight loss in the long term, especially for morbidly obese patients. However, recent evidence shows that bariatric surgery (BS) can revert T2DM in morbidly obese patients.

BS was first reported by Pories et al., in 1992. A systematic review and meta-analysis of the English literature reported complete resolution of T2DM (defined as discontinuation of all diabetes-related medications and blood glucose levels within the normal range) in 78.1% of cases. This percentage increased to 86.6% if patients reporting improvement of glycemic control were included. Diabetes resolution occurred concurrently in patients who experienced and average weight loss of 38.5 kg (55.9% of the excess weight). Although randomized, comparative clinical trials have not yet been carried out, the available data suggests that the clinical benefits of BS far outweigh the risks of complications, in morbidly obese individuals. However, the surgical mortality is 0.15%-0.35%, and there are considerable rates of early and late complications. Although all types of BS procedures improve T2DM by promoting weight loss, gastric bypass surgery and duodenal exclusion technique provides improvement in hyperglycemia and other metabolic abnormalities with the lowest rate of postoperative complications. It therefore seems the safest surgical option. The improvement in glycemic control occurs in patients with BMI both above and below 35 kg/m². The mechanism behind the correction of T2DM, though not fully understood, seems to be largely related to changes in anatomy, gastrointestinal hormone secretion, and various metabolic factors. Resolution of T2DM is associated with shorter duration of T2DM, dietary or oral antidiabetic agent therapy, major loss of weight after surgery and diversionary procedure.

Obesity as an important risk factor for Chronic Kidney Disease (CKD)

Various cross-sectional and cohort studies have consistently evidenced epidemiological associations between obesity, metabolic syndrome components (defined as the presence of 3 of the following 5 traits: abdominal obesity, impaired fasting glucose, hypertension (HTN), hypertriglyceridemia, and a reduced HDL cholesterol), and early CKD, understood as presence of albuminuria and/or a decreased glomerular filtration rate (GFR; < 60 ml/min/1.73 m²). Obesity is an important CKD risk factor. This implies that when obesity is reversed, many CKD risk factors are favorably influenced. Obesity can exacerbate other causes of CKD and has been associated with an acceleration of immunoglobulin A glomerulopathy (IgA nephropathy) as well as greater rate of kidney functional decline and proteinuria after unilateral nephrectomy when compared with subjects with a normal BMI level. Other obesity-related conditions such as dyslipidemia, hyperinsulinemia, HTN, DM, and other associated inflammatory states facilitate the progression of CKD. These obesity-related conditions are interdependent, and exacerbate kidney damage to a greater extent than what they would individually. Individuals with both HTN and DM have a 5- to 6-fold greater risk of developing end-stage renal disease (ESRD) compared with people with only HTN and no DM. Hsu et al., analyzed 2.691 community-based patient population the presence of DM, hemoglobin A1c, and serum cholesterol were significantly associated with increased risk for kidney impairment and thus associated with the development of CKD. Furthermore, obesity appears to independently increase CKD risk and progression in the setting of diabetes.

Diabetic nephropathy (DN) is the leading cause of ESRD and accounts for over 40% of new cases each year in the United States. Untreated DN is associated
with the fastest rate of progression in CKD with a yearly loss of GFR of 10 ml/min. The Multifactorial intervention and Cardiovascular Disease in Patients with T2DM Trial showed that intensive therapies directed at dyslipidemia, hyperglycemia, HTN, and microalbuminuria (MA) resulted in secondary prevention of cardiovascular disease (CVD) and a 50% risk reduction for onset of DN.31

MA, defined as an excretion rate of 30 to 300 mg per 24 hours, is the first manifestation of DN and is associated with risk of progression to ESRD and increasing risk of premature death. It is also recognized as an early independent risk factor for insulin resistance, DM, HTN and CVD-related morbidity and mortality. Reversal of early-onset glomerular changes and regression in CKD with associated complications has been shown in numerous lifestyle and intensive glycemic control studies.3 A positive correlation between urinary albumin excretion and body weight has been evidenced in both non-diabetic and diabetic overweight individuals. The effect of obesity on proteinuria is not bimodal, but a continuum that is directly related to increasing BMI.14 Obesity-induced MA has been found to precede histologic changes in the glomerulus and is hypothesized to be a result of increased intraglomerular pressure. In a retrospective analysis of the database of a population study on the impact of MA on renal and cardiovascular risk, found that the prevalence of MA in men increased from 9.5% in those with normal BMI (< 25) to 18.3% in those who were overweight, and to 29.3% in those who were obese, in women, the respective percentages were 6.6%, 9.2%, and 16.0%.15 On the other hand, a decrease in urinary protein excretion is associated with metabolic improvement and decreased cardiovascular risks.16 Accordingly, a 50% decrease in urinary protein excretion is associated with 18% decrease in cardiovascular risks.17 Therefore, reducing proteinuria is used as a surrogate outcome for evaluating CKD treatment.

The hemodynamic effects of overweight on kidney function and albuminuria are magnified in the presence of HTN, which itself is a clinical complication of obesity. A similar amplifier effect of obesity has been evidenced that even moderate weight loss can reduce proteinuria by 30% in overweight diabetics.18 There is, therefore, strong evidence that weight reduction, achieved by BS or dietary caloric restriction, decreases proteinuria in obese individuals, with and without T2DM.19,20 Additional long-term studies are needed to evaluate the durability of the beneficial effects of weight loss on kidney function and whether this is translated into an improvement in outcomes, such as slowing the development of ESRD. Weight loss will not only improve glycemic control but will also reduce the risk of CVD through beneficial effects on blood pressure, dyslipidemia, and serum markers of inflammation.16 The weight loss global should be both achievable and maintainable, the National Kidney Foundation (NKF) recommends a target BMI of 18.5-24.9 (i.e., within the normal range) for patients with diabetes and CKD.21 Weight management programs should comprise lifestyle measures (dietary restriction and increased physical activity) and anti-obesity medications if needed, coupled with appropriate support and counseling.22 However, this target is unrealistic for most overweight or obese patients with T2DM and is rarely achieved BS offers major improvement or complete remission of DM even independently of weight loss.7

Benefits of bariatric surgery on renal function

Bariatric Surgery in patients with normal renal function

BS has been associated with significant improvement in all parameters of renal function. Interestingly, the impact of BS on renal function occurs in patients both with and without established chronic renal impairment, as shown in table I. Serra et al., studied albuminuria levels before and after BS in 70 extremely obese patients with normal renal function. The patients has higher albuminuria levels (14.8 vs. 6.5 mg/24 h) than the control group with normal body weight.24 These levels decreased significantly to 12.8 mg/24 h, 12 months after BS (Roux-en Y gastric bypass, RYGB), after a drastic reduction in body weight (mean BMI reduction from 53.3 to 33.6 kg/m²). Navarro-Díaz et al., (25) followed up this group a further 12 months following surgery (2 years follow-up) and evidenced a further decrease in albuminuria (14.20 vs. 12.55 mg/24 h; p = 0.006). Other renal parameters (urea, creatinine, creatinine clearance, and proteinuria) were not significantly different from the 12 month follow-up stage. Agrawal et al., analyzed 94 obese patients who underwent RYGB. At baseline, 32 patients had T2Dm, 37 had metabolic syndrome, and 25 had obesity alone. At 12 months, there was improvement in lipid profiles and reductions in body weight, blood pressure, glycated hemoglobin levels, and in total cholesterol levels. At 12 months there was a significant decrease in urinary albumin to creatinine ratio (ACR) in the diabetic and metabolic syndrome groups, whilst the reduction was not significant in obese patients with obesity alone.26 The prevalence of MA (ACR ≥ 30 mg/g) after surgery was reduced only in the diabetic group (35.7% to 7.1%, p = 0.008). These studies suggest that improvement in renal parameters may be associated with improvement in diabetic status, but also that patients with diabetes and the metabolic syndrome may benefit most (from the renal perspective) by undergoing BS.
<table>
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<th>Type of surgery</th>
<th>Follow-up (weeks)</th>
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<th>ΔGFR (ml/min)</th>
<th>ΔPU (g/24 h)</th>
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<tr>
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<td>-9.5</td>
<td>-</td>
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RYGB: Roux-en-Y gastric bypass; LRYGB: Laparoscopic Roux-en-Y gastric bypass; RRYGB: Robotic Roux-en-Y gastric bypass; VBG: Vertical banded gastroplasty; N/S: Not specified; AGB: Adjustable gastric band; LSG: Laparoscopic sleeve gastrectomy; BMI: Body mass index; GFR: Glomerular filtration rate; PU: Proteinuria; MAU: Microalbuminuria; Cr: Serum creatinine; CrCl: Creatinine clearance; T2DM: Type 2 diabetes; MG: Membranous glomerulonephritis; FSGS: Focal segmental glomerulosclerosis; DN: Diabetic nephropathy; HTN: Hypertension; IgAN: IgA nephropathy; PP: Porphyria.
Having evidenced the benefit of RYGB in improving obesity-related hyperfiltration, Saliba et al., further investigated the effects of the bariatric procedure on tubular defects using urinary Cystatin C to urinary creatinin ratio. They confirmed that GFR is improved by RYGB; however, tubular damage was only reversed in non-diabetic obese patients. This may imply that the pathogenesis of renal disease in diabetics with excess weight may be a different from non-diabetic obese patients.

To evaluate the effect of restrictive BS on BMI and glycemic control, Chagnac et al. studied renal glomerular function in eight subjects with severe obesity (BMI 48.0 ± 2.4) before and after vertical banded gastroplasty (at 12-17 months follow-up). None of the patients had history of renal disease, and all had normal urea and creatinin values and negative proteinuria on dipstick testing. Nine healthy subjects served as controls. GFR and renal plasma flow (RPF) were determined by measuring inulin and r-aminohippuric acid (PAH) clearance. In the morbidly obese group, mean BMI fell from 48 to 32 kg/m² after bariatric surgery. Interestingly, GFR decreased from 145 to 110 ml/min and RPF from 803 to 698 ml/min. This finding of an apparent worsening in renal function (decreasing GFR) may represent an evolving injury. However, it could also demonstrate a reduction in the hyperfiltration which is the hallmark of obesity-related renal damage.

**Bariatric Surgery n patients with chronic kidney disease**

To the extent of our knowledge, there are only a few case reports and series of BS performed on CKD patients (table I). Alexander et al., monitored renal function pre- and post open gastric bypass in 45 morbidly obese non-transplant patients with CKD. Nine of these patients had resolution, improvement, or stabilization of their renal function after the procedure. Underlying renal disease in these nine patients were: primary focal segmental glomerulosclerosis (FSGS) (N = 5), glomerulonephritis (GN) (N = 2), and DN (N = 2). One of the patients with GN had complete remission of renal disease at 9 years follow-up. Two of the FSGS patients on dialysis were able to discontinue dialysis for 27 and 7 months. The remaining patients had stable renal function with a follow up for 2-5 years. There were no post-operative complications. Larger series of patients are needed to confirm these results. This series is very small and with the patients all suffering from different renal disorders it is difficult to draw firm conclusions, but the reversal of these diseases appears significant.

Proteinuria is an important and well-studied indicator of renal dysfunction and a number of case reports show an improvement in proteinuria after BS (table I). Izzedine et al. report a 25 kg weight reduction in an obese diabetic patient after RYGB and a reduction of proteinuria by 99% (6.3 g/24 h pre- vs. 0.07 g/24 h post-procedure). A further weight loss led to normalization of creatinine level. Cuda et al. also describe the effect of BS on a patient with CKD requiring multiple medications with significant proteinuria (1.15 g/24 h). Following laparoscopic RYGB, her weight was reduced 46 kg to a post-procedure BMI of 20.2. Her proteinuria declined to 0.27 g/24 h and she was able to stop all her medications. The impact of BS in an adolescent with chronic renal failure was evaluated by Fowler et al. The 17 year-old girl underwent laparoscopic RYGB, which reduced her BMI from 56.8 to 35.9 kg/m². Initially, her proteinuria was in the nephrotic range, but it normalized after BS, requiring no pharmacological therapy.

Surgical treatment of morbid obesity was also reported to stabilize creatinine during and 8-months period after gastric bypass in a 43-year-old man with chronic renal failure (creatinine 380 µmol/L before bypass and 353 µmol/L at 8 months after gastric bypass). Soto et al. reported a patient with IgA nephropathy and a creatinine of 539 µmol/Lat the moment of surgery. He required dialysis during the immediate post-operation, the serum creatinine had decreased to 141 µmol/L. Tafiti et al. report the impact of robotic gastric bypass on a patient on dialysis with ischemic chronic kidney impairment following type a aortic dissection. As an institutionally required bridge to renal transplantation, the patient underwent BS, which led to decrease in BMI from 52.5 to 37.6 kg/m². His creatinine fell from 362 µmol/L pre-operative to 168 µmol/L at 9 months following surgery and he was able to discontinue dialysis.

**Obesity and Dialysis**

Contrary to the evidence that obesity promotes the onset and, progression of CKD patients, obesity in dialysis patients appears to provide them a survival advantage (“reverse epidemiology”). This disparity may be due to the fact the patients on dialysis have an inherent survival advantage in comparison to the patients that have died before reaching ESRD and renal function replacement. The fact that the first report that describe this finding compared survival data with different follow-up in dialysis and non-dialysis patients (10 years for non-dialysis, and 4 years in dialyzed patients). Another reason for an advantage of obesity in dialyzed patients could be that higher BMI patients had better nutrition status. However, this survival advantage in obese patients is not found in all studies. Several studies have reported worse outcomes in dialysis patients who were overweight or obese. Kaizu et al. observed an increased mortality among a chronic hemodialysis (HD) population at the extremes of BMI levels producing a “U”-shaped mortality curve.
Obesity and Transplant

The apparently beneficial effect of obesity in dialysis patients has not been found to apply to transplant patients. The most extensive study on this topic was presented by Meier-Kreische et al. who analyzed data from the United States Renal Data System (USRDS) database between 1988 and 1997 involving 51,927 adult transplant recipients. The relative risk ratio for graft loss was approximately 1.4 in patients with a BMI > 36 kg/m² compared with those with normal BMI. Similar risk ratios were found for death censored graft loss (RR = 1.45 for BMI > 36 kg/m²), death with a functioning graft (RR = 1.36), and for cardiovascular-related complications (RR = 1.4). The best overall results were found in patients with a BMI of 22-24 kg/m². Cacciola et al., compared patients with BMI 30-34.9 to patients with BMI 35 or greater who underwent renal transplant (RT). The patients survival at 5 years for the lower BMI group was 95% and for the higher BMI group it was 79%. Graft survival at 5 years was 94.5% for the lower BMI group and 63% for the higher BMI group.

Bariatric surgery as a bridge to renal transplantation

It is well documented that obese patients have a higher incidence of wound complications and delayed graft function when they receive transplants. As a result of the increased incidence of surgical complications and death from CVD, most transplant center will not transplant patient with a BMI > 35 kg/m². Therefore, one of the major reasons for performing BS in morbidly obese dialysis patients may be to improve their comorbidities and prepare them for transplantation. Table II shows BS studies reporting BS on CKD before and after receiving RT. Takata et al. report results after laparoscopic RYGB in seven ESRD patients without perioperative complications of death. After an average 15 months follow-up, mean excess body weight loss was of 61% and all patients were accepted for transplant. Reviewing the USRDS (2001-2004), Modanlou et al. identified 29 BS operations performed on patients on transplantation waitlist, and 72 BS performed on patients waiting to be enrolled in the transplant list. Comparison to published clinical

<table>
<thead>
<tr>
<th>Study reference</th>
<th>Population</th>
<th>Type of surgery</th>
<th>Follow-up (weeks)</th>
<th>ΔBMI (kg/m²)</th>
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<tr>
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<td>8 aRT; 3 bRT</td>
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<td>RYGB</td>
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<td>-</td>
<td>DM resolution. Cyclosporin requirement increased 33% (p = NS)</td>
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<td>-4.7</td>
<td>DN (N = 11); HTN (N = 13); GNC (N = 14); Other (N = 63); DM (N = 30); DN (N = 31); HTN (N = 12); GNC (N = 20); Other (N = 24); DM (N = 35)</td>
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<tr>
<td>Koshy&lt;sup&gt;9&lt;/sup&gt;</td>
<td>3 bRT; 60</td>
<td>AGB</td>
<td>60</td>
<td>-5.7</td>
<td>DN (N = 2); FSGS (N = 1)</td>
</tr>
<tr>
<td>Szomstein&lt;sup&gt;10&lt;/sup&gt;</td>
<td>5 aRT</td>
<td>LRYGB (N = 4); Gastrectomy (N = 1)</td>
<td>24</td>
<td>-20.3</td>
<td>PKD (N = 1); GNC (N = 1); ND (N = 3)</td>
</tr>
</tbody>
</table>

trials of BS in populations without kidney disease indicates similar weight loss (approximately 60%) but higher post-BS mortality (3.5%) in this USRDS sample. Twenty of the 29 BS cases performed on patients on list proceeded to transplantation, with a median waiting time of 17 months. It is unlikely they would have been transplanted without their bariatric surgery. The remaining nine patients had not received transplant by the end of follow-up.

Concerns exist regarding BS and the resultanting malabsorption, that can affect the pharmacodynamics of immunosuppressive medications, especially with RYGB. Szomstein et al.36 however reported no need for increasing levels of cyclosporine in their series, whilst Alexander et al.36 reported a modest increase in dosage for some patients following RYGB, indicating that extra vigilance may be required in immunosuppressive therapy in post-BS RT recipients.

In addition, there are concerns about providing highly technical BS in patients who have received a RT. Nevertheless, both Szomstein et al.36 and Alexander et al.36 report the safety of performing BS on RT recipients with either group’s patients suffering from anastomotic leak, hernia or graft loss. These reports indicate that the provision of RYGB in RT recipients is both safe and efficacious.

**Risks of bariatric surgery on renal function**

**Acute Kidney Injury (AKI)**

The development of post-operative AKI is a well-recognized and highly concerning complication of BS. The use of general anesthesia can induce a reduction in renal blood flow in about 50% of patients, which can further exacerbate advanced CKD and promote delayed clearance of medications and anesthesia. The perioperative period is a time of increased stress originating from fluid and hemodynamic shifts that can lead to AKI. This is of special concern if there is some degree of underlying CKD.

In CKD patients, obesity is associated with higher perioperative death rates. Approximately 1.2% of patients undergoing general surgery develop AKI, but this can be as high as 7% in the DM population. Acute perioperative kidney failure is associated with an increased risk for acute mortality of 40% to 90%. A prospective study of 109 patients with a baseline GFR of 82 ml/kg/min that underwent BS, found that the rate of AKI (defined as a rise in serum creatinine more than 25% above baseline or 0.5 mg/dl) was 6.4%. The majority of these cases had primary cardiopulmonary complication such as myocardial infarction, stroke, heart failure, or venous thromboembolism. The risks of AKI in patients with more advanced CKD undergoing BS are unknown.

Risk factors for the development of kidney injury included increased weight several medical co-morbidities, and the concurrent administration of nephrotoxic medications such as non-steroidal anti-inflammatory agents and angiotensin converting enzyme inhibitors. Both rhabdomyolysis and nephrolithiasis are noted to be common factors in post-bariatric surgery AKI.59

**Rhabdomyolysis**

Although rhabdomyolysis in BS has been described as a rare complication in some case series, it was diagnosed in 22-77.3% in one report.5 A major risk factor for the development of rhabdomyolysis is the length of operative time. The presence of medical co-morbidities is a further risk factor for the development of rhabdomyolysis following BS, as were HTN and DM.59

**Nephrolithiasis and oxalate nephropathy**

Obesity itself appears to be a risk factor for stone formation. Early cross-sectional studies evidenced that the prevalence of nephrolithiasis was related to BMI. Furthermore, larger body size is associated with higher urinary urate and oxalate excretion, which may further promote calcium-oxalate stone formation.59 Other important potential precipitating factors were decreased urinary volume and decreased urinary citrate. There is general agreement in the literature that hyperoxaluria is a characteristic feature of post-bariatric renal stones and is associated with a reduction in both urinary citrate concentration and urine volume.59

In an attempt to investigate a possible difference between malabsorptive and restrictive bariatric procedures, a group of 18 patients undergoing restrictive obesity surgery [sleeve gastrectomy (n = 4) and gastric banding (n = 14)] had urinary metabolites measured over a 2-months period. The group was compared to controls 8n = 168 = adults with kidney stones (n = 1,303) and RYGB patients (n = 54). There was no significantly increased risk for kidney stone formation when compared to a control cohort of both stone- and non-stone forming subjects. Furthermore, over a period of 2 months, the urinary oxalate excretion of the restrictive group was significantly less than that of the RYGB cohort (n = 54), suggesting that restrictive techniques of BS may be less lithogenic than malabsorptive methods.59

The lithogenicity of BS (in particular RYGB) is thought to be multifactorial. Lipid malabsorption due to the reduction of the gastric and small bowel capacity enhances the saponification of calcium in the gut, which limits the amount of available calcium to bind oxalate in the colon. In addition, as the absorption of bile salts is reduced, their concentration in the colon is larger and contributes to enhance the colonic mucosa’s permeability to oxalate. This further leads to increased oxalate absorption and subsequent renal excretion. Studies have also suggested that oxalate processing
bacteria in the gut may play a role. Colonization with *Oxalobacter formigenes* has been shown to be associated with lower urinary oxalate secretion whereas antibiotic-associated decolonization can increase these levels.53

The treatment of nephrolithiasis in patients with bariatric surgery is standard and comprises removal of the stones and prevention of recurrence. Recent guidelines suggest that prophylactic dietary modification is the current best strategy. A low oxalate diet in combination with calcium supplements (as oxalate binding agents) has been shown, to be effective in protecting post-RYGB patients with enteric hyperoxaluria from developing nephrolithiasis. Additionally, administration of oral calcium is recommended because calcium forms a complex with free oxalate and limits its absorption.53

Oxalate nephropathy is a complication of BS that is frequently under-reported. It is characterized by tubular deposition of calcium oxalate crystals, which can lead to AKI and CKD. The main risk factor for calcium oxalate deposition is hyperoxaluria; however, the presence of fluid depletion and previous renal insufficiency markedly increase the risk of renal failure. The prognosis of oxalate nephropathy after RYGB is poor and leads to ESRD in the majority of patients. Nasr et al., reported 11 patients who developed oxalate nephropathy after RYGB. Eight patients were morbidly obese, three patients were intervened due to gastric adenocarcinoma. Their conclusion was that oxalate nephropathy is an under-recognized complication of RYGB, and patients, with pre-existing renal disease may be at higher risk of developing it.53 There are no guidelines for the management of oxalate nephropathy after RYGB. Of note, renal biopsy should be considered in patients whose renal function deteriorates after RYGB.53 Whether the reversal of bypass surgery leads to improvement in renal function is controversial and needs to be clarified with further research.

Conclusions

Since obesity is a major risk factor in the natural history of CKD and CVD risk, it is understandable that sustained and substantial reductions in body fat reduces the risk for both CKD and CVD. There is evidence that BS resolvers or significantly improves body fat and metabolic syndrome as opposed to simple morbid obesity. There is little information on patients with established kidney disease undergoing BS either before or after RT. However, these studies do indicate an important effect of RYGB in this “at-risk” population. Prospective studies are needed to evaluate the effect of the diverse types of BS on renal function in obese CKD patients.

Evidence shows that BS has potential to improve outcomes in chronic renal impairment. BS may enable obese patients with ESRD to be eligible for a renal transplantation, and in itself may slow down CKD progression. However, more data is required to compare obese patients who do and do not undergo BS and examine dialysis requirements, transplant-related outcomes, and overall survival. Future research will address how the timing of BS may affect transplant-related outcomes.

Whereas diabetes is strongly associated with increased morbidity and mortality following BS, the benefits of bariatric operations in morbidly obese diabetic patients can hardly be overlooked. Consequently, conventional bariatric procedures are increasingly being used worldwide to treat T2DM in association with obesity, and among less obese or merely overweight patients.

References