Renal Complications After Bariatric Surgery

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Superficially, it might be said that the function of the kidneys is to make urine; but in a more considered view one can say that the kidneys make the stuff of philosophy itself.

—Homer Smith

10.1 The Relationship Between Obesity, Diabetes, and Renal Disease

The pandemic crisis of obesity has worsened over the last several decades. Obesity increases the risk of diabetes and hypertension and is often part of a larger public health crisis known as the metabolic syndrome [1]. The metabolic syndrome can have a detrimental impact on an individual's renal function. The literature estimates that in 14–30% of those with chronic kidney disease (CKD), obesity plays a pathogenic role and a fifth of these patients have at least stage II obesity [2, 3]. Furthermore, epidemiological investigations have demonstrated the correlation between each component of the metabolic syndrome and increased risk of developing CKD. The overall metabolic health of an individual is more indicative of the risk of CKD development as evidence points out that metabolically healthy individuals with obesity have lower risk of CKD development than metabolically unhealthy individuals without obesity [4]. Obesity has also been found to increase the risk of nephrolithiasis and renal cell cancer [3]. Mechanisms by which obesity leads to renal dysfunction include obesity-mediated hypertension, insulin resistance, glomerular

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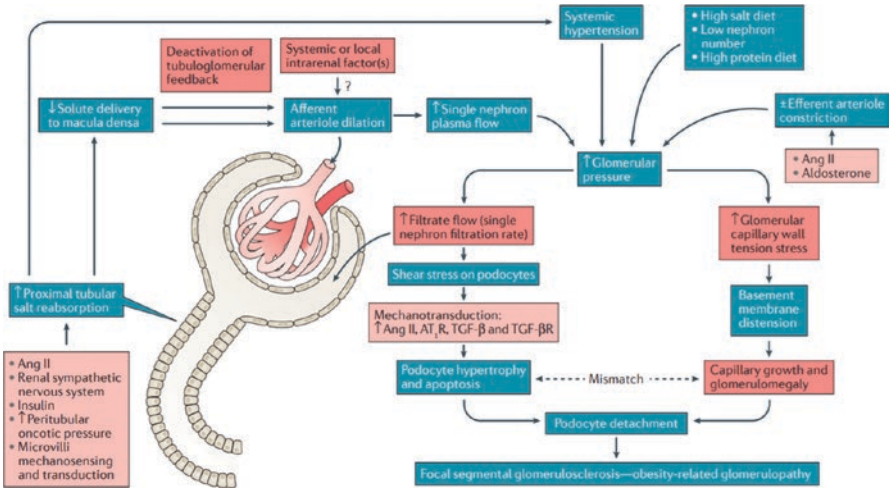


Fig. 10.1 Obesity-related glomerulopathy. Hemodynamic alterations in obesity: primary dilatation of the afferent arteriole and variable constriction of the efferent arteriole via activation of angiotensin II (Ang II) and aldosterone contribute to increases in single nephron plasma flow, glomerular intracapillary hydrostatic pressure, and filtration rate. The major driver of afferent arteriolar dilatation is unknown, but deactivation of tubuloglomerular feedback via increased proximal tubular salt reabsorption and decreased delivery to the macula densa likely has a role. A host of factors, including Ang II, the renal sympathetic nervous system, insulin, an increase in postglomerular oncotic pressure due to increased filtration fraction, and mechanosensors of tubular flow rates, mediate the increased tubular reabsorption of sodium. The increase in filtrate flow (single nephron filtration rate) in turn promotes glomerular capillary wall stretch tension, glomerulomegaly, and maladaptive podocyte stress leading to obesity-related glomerulopathy and focal segmental glomerulosclerosis. *AT1R* type 1 angiotensin II receptor, *TGF-β*, transforming growth factor β, *TGF-βR* TGF-β receptor. Adapted with permission from *Nat Rev Nephrol* 12, 453–471 (2016)

hypertrophy, activation of the renin–angiotensin–aldosterone system, inflammation, and adipocytokine dysregulation [3].

Obesity affects the kidney through a process known as obesity-related glomerulopathy (ORG, Fig. 10.1). Obesity causes hemodynamic changes at the level of the glomerulus by reducing preglomerular vascular resistance and increasing the glomerular filtration rate (GFR). This results in glomerular hyperfiltration, known to be a major cause of ORG [5]. The resultant glomerular hypertension leads to glomerulomegaly, mild effacement of podocytes, stretching of the microvasculature in this region, and eventual microalbuminuria. The pathologic findings of ORG are focal segmental glomerulosclerosis (FSGS) lesions in the perihilar region, mesangial and tubular cell lipid deposits, and podocyte effacement from glomerular hypertrophy. In patients with obesity without diabetes, diabetic-like renal changes have been found, focal mesangial sclerosis and thickening of tubular and basement membranes [6].

Obesity-related hyperfiltration may also be impacted by increased glucose and sodium absorption in the proximal convoluted tubules via the sodium–glucose cotransporter proteins (SGLT1 and SGLT2). Obesity can cause a decreased sodium load at the distal tubule, and feedback to the macula densa promotes afferent arteriole vasodilation and subsequent glomerular hyperfiltration. Inhibitors of SGLT2 have been shown to reduce albuminuria and GFR, giving further credence to the hypothesis of a renal tubular origin of ORG [7, 8].

The most common clinical manifestation of obesity-related renal disease is proteinuria, which can be, but is usually not, detected in the nephrotic or massive range (>3.5 g/day and >20 g/day, respectively) [9, 10]. There is likely a slow progression of proteinuria over time and metabolic compensation is allowed that limits the development of nephrotic syndrome (hypoalbuminemia, edema, and hyperlipidemia). Potential mechanisms responsible for ORG-specific differences from nephrotic syndrome may be increased hepatic synthesis of albumin over time and also tubular handling of filtered proteins that may change in the setting of hyperfiltration [5]. This clinical distinction in ORG is important for clinicians to be aware of when patients with obesity are detected to have proteinuria for the most accurate diagnostic and therapeutic interventions. Furthermore, studies have shown that renal biopsies at the time of bariatric surgery reflect ORG-lesions even without clinical manifestations of proteinuria or renal derangements [11].

10.2 Early Postoperative Complications

Acute kidney injury (AKI) can complicate the postoperative course after metabolic surgery, and its incidence is approximately 1% [12]. The etiology of perioperative AKI after bariatric surgery is multifactorial in the obese population and individuals with pre-existing hypertension, diabetes, and renal disease are at increased risk of perioperative AKI [13–15]. There is a three- to sevenfold increase in postoperative AKI in patients undergoing noncardiac surgery with obesity compared to individuals without obesity [16]. Morbidity and mortality following bariatric surgery in the setting of acute renal dysfunction, especially for severe cases requiring dialysis support, is increased by 6.5-fold [17, 18].

A study published by Hanipah et al. in 2018 explored the incidence of postoperative AKI in 42 of their 4722 metabolic surgery patients along with the major causes and long-term effects on renal function. Acute kidney injury occurred due to prerenal causes in 88% of patients and renal causes in 12%. Nine patients (21%) required hemodialysis support in the postoperative period due to septic shock ($n = 7$), bleeding ($n = 1$), and worsening pre-existing CKD stage 5 ($n = 1$). Median follow-up was 28 months and 90% had a return to baseline renal function. Of the four patients who had abnormal renal function at follow-up, three had CKD stages 4 and 5 prior to surgery and required permanent dialysis, and one developed CKD stage 3 postoperatively due to short gut syndrome after multiple surgeries. This study concluded that most patients have a return to normal baseline renal function after postoperative

AKI, however, those with pre-existing renal disease are at high risk for persistent renal dysfunction [12].

Koppe et al. compared the incidence of AKI in bariatric surgery patients (n = 2643) compared to a matched, nonsurgical cohort (n = 2595) using a large, prospectively maintained database in the United Kingdom. This study found a low incidence of AKI (five events) within the first 30 days following surgery and a protective effect of bariatric surgery compared to controls beyond 30 days during the 3-year follow-up period [19].

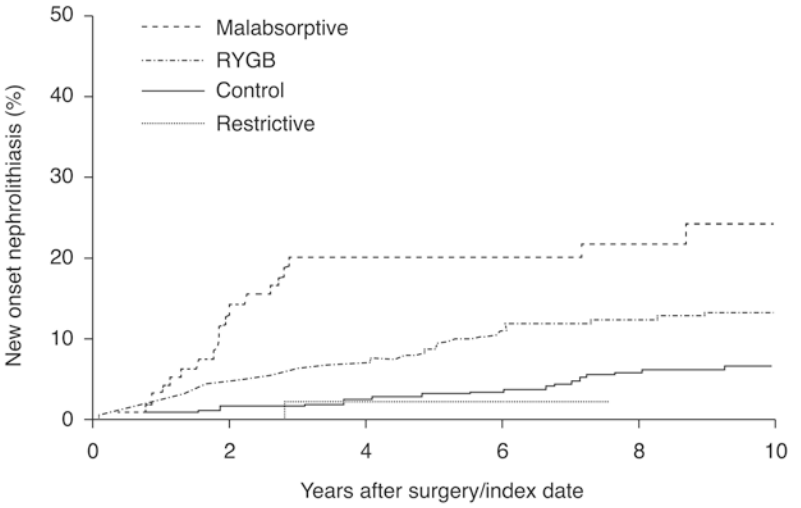
A multicenter study based out of Australia evaluated 590 bariatric surgery patients who were admitted to the intensive care unit (ICU) postoperatively. This study found that patients who developed AKI in the ICU (17%), had increased peak plasma creatinine concentrations, hospital and ICU lengths of stay compared to those ICU patients without AKI. While most of these AKI episodes (76%) were mild, a single episode of AKI in the ICU postoperatively was associated with higher long-term mortality [13].

Appropriate management of postoperative AKI in the bariatric and metabolic surgery population involves early identification of renal dysfunction, aggressive hydration with intravenous fluids for prerenal causes such as dehydration, bleeding, and hypovolemia from sepsis. Prompt treatment for infectious etiologies and septic shock is also warranted to avoid multiorgan dysfunction and further metabolic derangements that make renal function worse. Renal causes of AKI such as rhabdomyolysis and contrast nephropathy should also be treated expectantly.

10.3 Nephrolithiasis

Obesity is a known risk factor for nephrolithiasis. Different metabolic surgery procedures are also associated with nephrolithiasis to varying degrees: purely malabsorptive procedures (22–28%), Roux-en-Y gastric bypass (RYGB) (7–13%), and lowest in restrictive procedures [SG and adjustable gastric banding (ABG)] (Fig. 10.2) [20]. Time to renal stone development after bariatric surgery ranges from 1.5 to 3.6 years [21–23]. Prior history of stones before surgery increases the risk of postoperative stone development compared to those without a history (42% vs. 14%, respectively, HR > 4.1, $p < 0.0001$) [24]. De novo stone formation after RYGB in those with no prior stone history ranges from 3 to 8% [23, 25].

Several components are at play in the pathogenesis of nephrolithiasis after metabolic surgery—namely hypovolemia, hyperoxaluria, hypocitraturia, aciduria, and supersaturation of the urine with calcium oxalate [26, 27]. Oxalate is an endogenous byproduct of amino acid metabolism and is absorbed by the stomach, small intestine, and colon. Its absorption is increased in malabsorptive states and secondary enteric hyperoxaluria (urinary excretion of >40–45 mg/day) develops due to increased absorption of oxalate from the intestine—inflammation and bile salts promote mucosal permeability. Calcium usually binds oxalate and is excreted in the stool. However, due to the presence of non-absorbed fatty acids binding calcium in enteric hyperoxaluria in malabsorptive states, more oxalate is available downstream



No. at risk						
Malabsorptive	101	77	58	47	36	27
RYGB	563	502	408	293	208	94
Control	729	673	572	416	282	135
Restrictive	55	54	36	18	0	0

Fig. 10.2 Risk of new-onset nephrolithiasis after bariatric surgery. The risk of incident stones was greater after RYGB or malabsorptive bariatric procedures compared with that of matched obese controls. Patients with restrictive procedures were not at increased risk. Adapted with permission from Kidney International (2015) 87, 839–845

in the colon to be passively absorbed into the bloodstream and eventually filtered and excreted by the kidneys [28, 29].

Malabsorptive procedures (RYGB, jejunoileal bypass, and biliopancreatic diversion with duodenal switch) have the highest rate of nephrolithiasis, postoperatively. In the Rochester Epidemiology Project, all patients who underwent an RYGB had higher urinary oxalate levels, and those who developed renal stones had the highest levels along with supersaturation of calcium oxalate. The number of other types of renal stones does not change significantly (hydroxyapatite, struvite, and uric acid) [24]. The makeup of the colonic flora can also have an impact on the clearance of luminal oxalate. *Oxalobacter formigenes* (*O. formigenes*) is a Gram-negative anaerobe found to be associated with lower urinary oxalate levels [30]. After malabsorptive surgery, the alteration in the gut microbial flora that reduces *O. formigenes* in addition to increased fecal fat content can promote increased oxalate absorption and lead to a higher incidence of nephrolithiasis [30, 31].

Hypocitraturia after metabolic surgery is less common than hyperoxaluria with a 24–63% incidence in the literature [20]. Citric acid is a weak acid made endogenously from the tricarboxylic acid cycle and also comes from fruits and vegetables in the diet. Its dissociated anion is citrate, which forms soluble complexes with

calcium in the urine and prevents precipitation of calcium oxalate and calcium phosphate. In acidosis, the mitochondrial use of citrate increases, leading to increased renal absorption and hypocitraturia of <320 mg/day. Assuming a 2-L urinary output daily and normal urine pH and potassium levels, 640 mg/day is the urine citrate in normal, healthy individuals [32].

Obesity is associated with hypercalciuria, which also promotes stone formation. RYGB has been associated with hypocalciuria and this can exert a protective effect on stone formation by preventing supersaturation of calcium oxalate in the urine. Valezi and colleagues demonstrated in 151 RYGB patients that one-fifth of those with hypercalciuria preoperatively had none postoperatively [33]. Urinary volume decreases significantly after metabolic surgery and is a major driver of urinary crystallization. One study found the average drop in 24-h urine volume to go from 1.8 L/day to 1.4 L/day, and this is consistent with other findings of a sustained decrease in volume from 2100 mL/day to 750 mL/day [34, 35]. Aciduria promotes uric acid supersaturation and uric acid stones but these are a less common occurrence after metabolic surgery compared to calcium oxalate stones, 1.5% vs. 94%, respectively [24].

The jejunoileal bypass in the 1970s proved to be littered with complications and was eventually abandoned with a 28% risk of nephrolithiasis and a 9% risk of renal insufficiency according to a 15-year longitudinal study [36]. The now more commonly performed metabolic surgeries have a varied risk of nephrolithiasis (Fig. 10.2) [24]. Extensive gastrointestinal bypass procedures have a documented higher risk of nephrolithiasis compared to restrictive procedures. A retrospective database review of 4639 patients following RYGB compared to matched obese controls revealed a 7.65% vs. 4.63% nephrolithiasis risk (odds ratio of 1.71) and a mean time to developing renal stones of 1.5 years [37]. There is an increase in stone risk also with more distal RYGB procedures [21]. Lieske and colleagues prospectively matched 762 bariatric patients with obese controls with similar baseline nephrolithiasis incidence of 4% and 4.2%. The development of new stones tripled in the bariatric group postoperatively to 11.1% vs. 4.3% at a mean follow-up of 6 years. Baseline stone type in these two groups was largely calcium oxalate 73% vs. 65% and increased postoperatively to 94% calcium oxalate. In patients undergoing malabsorptive procedures, those at highest risk for stones are also at highest risk for CKD (hazard ratio of 1.96, $p < 0.03$), although this distinction is not detected when all bariatric procedure types are combined [24].

Restrictive procedures have demonstrated a much lower risk of nephrolithiasis compared to malabsorptive procedures, and that risk approaches that of nonsurgical matched obese controls [24, 38]. Semins and others have demonstrated that AGB patients have an even lower incidence, 1.49% vs. 5.97% that is consistent beyond 2.5 years [39]. Restrictive procedures also are associated with hypovolemia, but this effect is likely countered by the hypocalciuria and the low stone risk is maintained [20].

Mitigation and management of nephrolithiasis can be achieved to improve patient outcomes. Hyperoxaluria can be managed with a low-fat diet that would decrease the fatty acid load and promote calcium oxalate binding. A low oxalate diet

and calcium supplementation would also decrease the oxalate load in the gut and decrease the incidence of hyperoxaluria. Adequate daily hydration keeps urinary volume closer to baseline levels and decreases the risk of crystallization and supersaturation of calcium oxalate in the urine [40]. Hypocitraturia can be treated with potassium citrate salts and also calcium citrate, which increases urinary citrate levels, increases hypercalciuria, and also increases the calcium load in the intestinal lumen to bind oxalate. Probiotics could potentially repopulate the gut flora with oxalate reducing species, such as *O. formigenes*.

Procedural interventions are mainly shockwave lithotripsy and ureteroscopy as reported by Matlaga and colleagues. In this study, 355 RYGB patients who developed urinary calculi in the treatment cohort were more likely to undergo shockwave lithotripsy (1.75% vs. 0.41%) or ureteroscopy (2.11% vs. 0.58%). The odds ratios for RYGB patients to develop stones and subsequently need procedures were 1.71 and 3.65, respectively [37].

Further opportunities exist for advancing our knowledge of the mechanisms for nephrolithiasis and preventing this risk in metabolic surgery patients. The SLC26 gene family encodes oxalate transport proteins in the intestines that may have altered function following RYGB. Risk stratification preoperatively of patients at highest risk for nephrolithiasis can be implemented and influence the recommended and chosen procedure type [32].

10.4 Safety of Bariatric and Metabolic Surgery in Patients with Chronic Kidney Disease

The stage of CKD does not significantly affect 30-day mortality, but there is a positive correlation between stage of renal dysfunction and postoperative complications, albeit low [41]. Thirty-day mortality for patients with ESRD range from 0.4 to 0.7% [42, 43]. The impact of varying degrees of renal dysfunction on short-term bariatric surgery outcomes was studied by Saleh and colleagues [44]. Using the American College of Surgeons National Surgical Quality Improvement Program database, over 64,000 patients were retrospectively evaluated with varying degrees of CKD based on estimated GFR (eGFR): stage I (61.7%), stage 2 (32%), stage 3 (5.3%), and stages 4 and 5 (1%). There was an increasing trend in overall and major complications with increasing renal insufficiency, however, there was no statistical significance. There was only a significant difference in the RYGB group who had stage I vs III renal disease for overall complications and stage I vs IV for major complications ($p < .001$).

Cohen and others conducted one of the largest retrospective cohort studies [45] using the Metabolic and Bariatric Surgery Accreditation and Quality Improvement Program to determine the effect of CKD and ESRD on short-term postoperative outcomes in bariatric surgery. Using matching techniques to account for differences in patient characteristics, they evaluated 323,034 bariatric surgery patients without CKD, 1694 with CKD, and 925 with ESRD. There was an increase in 30-day reoperation rate with an odds ratio of 2.25 and 3.1 for CKD and ESRD, respectively, and

an increased mortality rate with an odds ratio of 11.59 for ESRD patients. Also, men with CKD had higher readmission rates compared to men without CKD, while women in both groups had similar rates in this category. Overall adverse outcomes were considered low at less than 15% and bariatric surgery was still deemed safe for patients with CKD and ESRD. The mortality rates for those with renal disease were comparable to those in the literature without bariatric surgery. This study was reflective of the current trends in bariatric surgery with approaches being minimally invasive and the majority of patients in each group undergoing SG. It was limited by the lack of delineation in renal dysfunction between patient groups and the limited data from the database not capturing specific parameters such as creatinine levels and proteinuria [45].

A longitudinal population-based study of Medicare beneficiaries who underwent bariatric surgery from 2006 to 2016 compared the postoperative outcomes of those with and without ESRD [46]. Over the course of the study period, there was a 9-fold increase in patient volume and an 1.5-fold increase in ESRD prevalence. Readmission rates and length of stay were higher for those with ESRD than those without. During this time there was also a surge in the number of SG procedures from less than 1% to 84%. This study captures the current trends in procedure type across the country and captures a large proportion of the ESRD community that is served by Medicare.

Metabolic and bariatric surgery is safe in select patients with CKD and should not be perceived as a contraindication for surgery. There is a slightly higher risk for early postoperative complications in patients with CKD but long-term evidence shows a benefit in overall renal function.

10.5 Considerations in Transplant Candidates/Recipients

Obesity increases the risk of CKD and eventually contributes to development of ESRD [47]. As defined by the United States Renal Data System (USRDS), ESRD patients are formally registered to receive hemodialysis or transplantation as a form of renal replacement therapy [48]. The incidence of ESRD at the end of 2016 according to the USRDS was 1887 per million individuals and the two primary causes were diabetes and hypertension. Obesity is the most preventable risk factor in ESRD and 60% of affected individuals are either overweight or obese [49, 50]. Renal transplantation for ESRD patients have clear benefits, however, many patients with class III or higher obesity are not able to be listed for transplantation due to the associated relative and absolute contraindications at some institutions (BMI greater than 35 and 40, respectively) [51, 52].

Bariatric surgery serves as an effective bridge to transplantation for ESRD patients who are unable to be listed due to class III or higher obesity, and this is a more reliable weight loss strategy than nonoperative management [53]. A registry-based study from a single center in Florida by Modanlou et al. reported that 72 obese patients (BMI 38 ± 12) who underwent bariatric surgery had an average time to activation on the transplant list of 16 ± 13 months (n = 72) and an actual time to transplantation from bariatric surgery of 17 ± 11 months (n = 29) [53]. Al-Bhari

et al. at a single center in Florida retrospectively reviewed the outcomes of 16 patients on hemodialysis who underwent bariatric surgery from 1998 to 2016. Median follow-up was 2.8 years (range 1–10), preoperative BMI was 48 ± 8 kg/m^2 and postoperative BMI was 31 ± 7 kg/m^2 with an average percent excess body weight loss of 62 ± 24%. At the time of publication, four patients (25%) had undergone renal transplantation at 4.3 ± 1.4 years post-bariatric surgery, five patients were currently listed, five patients were still not listed due to persistent comorbid conditions, and two patients died due to comorbidities. Waiting times for transplantation in the bariatric surgery population continue to be due to a shortage of organs and regional factors such as pretransplantation work up [54].

Transplant recipients who are obese have a higher risk of posttransplant diabetes, surgical site complications, delayed graft function, and higher mortality due to obesity-related comorbidities [55, 56]. Remission or mitigation of obesity-related comorbidities through metabolic surgery can improve outcomes for renal transplant recipients.

10.6 Risk Reduction After Metabolic Surgery

Improving the major risk factors of CKD through metabolic surgery can significantly address the global health and economic strains that ESRD carries. Long-term evidence demonstrates that metabolic surgery significantly reduces the overall risk of renal dysfunction in patients with significant metabolic risk factors.

The investigators of the STAMPEDE trial published their long-term 5-year results after randomizing patients with T2D to receive either medical therapy or RYGB or SG. The primary endpoint of glycated hemoglobin less than 6% without diabetes medications was met by 5% of participants in the medical cohort versus 29% in the surgical cohort [57]. In addition to improved glycemic control, patients who underwent metabolic surgery had a significant decrease in the use of medications for diabetes, hypertension, and dyslipidemia. These long-term results suggest that the overall metabolic improvement with surgery compared to medical therapy alone leads to reduced risk of eventual renal dysfunction that the metabolic syndrome causes.

In the prospective, matched Swedish Obese Subjects study, patients with obesity and diabetes who underwent bariatric surgery compared to usual care experienced higher rates of diabetes remission, which subsequently correlated to reduced incidence of microvascular complications after 15 years. When analyzing these outcomes based on glycemic status, surgery was found to have the greatest risk reduction among participants with prediabetes compared to usual care. In those with prediabetes who underwent surgery, the risk of renal microvascular complications was reduced even among those who develop diabetes during follow-up [58].

Aminian and colleagues evaluated 131 patients with diabetes and the impact of RYGB on the long-term risk reduction of various end-organ complications using various risk prediction models. Median follow-up was 6 years after RYGB, and excess weight loss was 60.7 ± 25.1% with a diabetes remission rate of 61%.

Significant percentages of patients had other metabolic syndrome components to fall within appropriate range at follow-up according to the American Diabetes Association criteria: glycated hemoglobin (85%), LDL (73%), and blood pressure (63%). The predicted relative risk reduction for cardiovascular disease (CHD, Stroke, and PVD) was 27% and for moderate–severe chronic kidney disease was 45% [59, 60].

Other studies have also documented strong evidence for the remission of metabolic syndrome components. Adams and colleagues report a 62% diabetes remission after RYGB at 6 year follow-up [61]. The Swedish Obese Subjects study after 10-year follow-up found improved recovery for diabetes, hypertriglyceridemia, low HDL, hypertension, and hyperuricemia with metabolic surgery [62]. Brethauer et al. who investigated 217 patients with diabetes after metabolic surgery also found a diabetes remission rate of 50%, improvement in 34%, and no change in 16%. The usual normo-albuminuria to albuminuria transition rate of 2–4% per year reported in the literature, was less than 1% per year after metabolic surgery in this small study. Regression of established diabetic nephropathy was seen in approximately half of patients [63, 64].

Reducing the incidence of microvascular complications from diabetes are critical outcomes to measure the efficacy of metabolic surgery compared to medical therapy. A large multicenter-matched cohort study retrospectively evaluated adults with T2D and severe obesity. There were 4024 patients who had bariatric surgery compared to 11,059 nonsurgical controls. The surgical cohort demonstrated a lower incidence of composite microvascular disease as well as nephropathy at 1, 3, 5, and 7 years after the index date. Specifically, at 5 years, incident composite microvascular disease and nephropathy was 59% lower with surgical treatment [65].

Similarly, another large, retrospective, matched-cohort study from the Cleveland Clinic Health System compared metabolic surgery and usual care for patients with T2D and obesity. The primary outcome was incidence of extended major adverse cardiovascular events (MACE): all-cause mortality, coronary artery events, cerebrovascular events, heart failure, nephropathy, and atrial fibrillation. Patients who underwent metabolic surgery had a 40% reduction in MACE (hazard ratio, HR, of 0.61) and a 60% reduction in risk of nephropathy (HR 0.40) in 8 years (Fig. 10.3) [66].

Studies have also shown that metabolic surgery reduces the risk of CKD, stage 3 or higher, from progressing to kidney failure. Funes et al. reported a risk reduction of 70% at 2 years and 60% at 5 years [67]. These studies demonstrate the profound impact that metabolic surgery has on obesity-related renal dysfunction when compared to medical therapy. Substantial and sustained weight loss accounts for much of the metabolic, hemodynamic, and neurohormonal changes that occur after metabolic surgery. However, there is growing evidence that some of these significant changes are weight independent [68–70]. The risk reduction that metabolic surgery affords to individuals with obesity and metabolic risk factors makes this treatment a powerful tool going forward to treat and prevent chronic diseases that affect the kidneys and other organ systems.

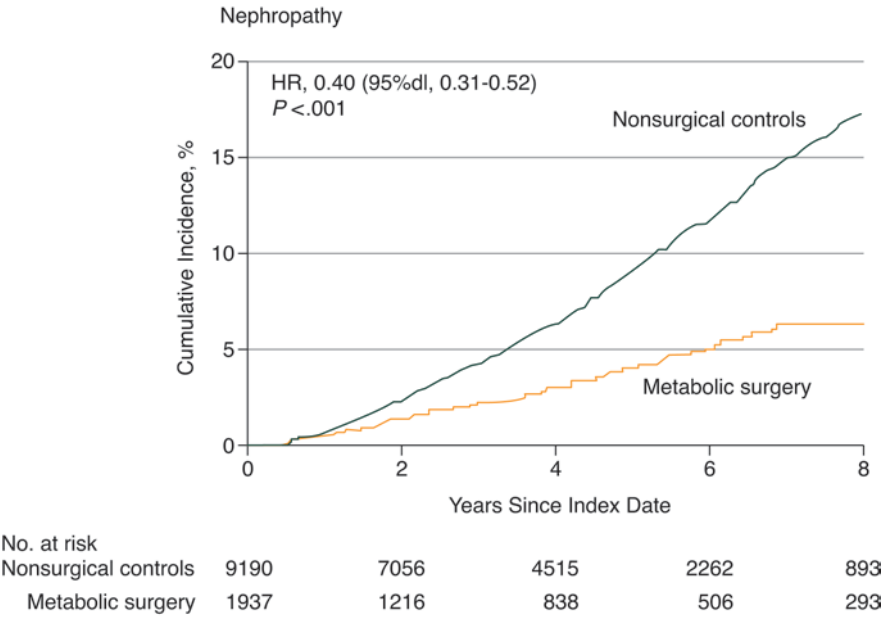


Fig. 10.3 Kaplan-Meier curve of the cumulative incidence of nephropathy at 8 years. Adapted with permission from *JAMA*. 2019;322(13):1271–1282

10.7 Improvement of Kidney Function After Metabolic Surgery

There is a close relationship between obesity and albuminuria, a marker of kidney damage defined as a urinary albumin-to-creatine ratio (UACR) of greater than 30 mg/g. Albuminuria is also a known risk factor for renal and cardiovascular disease but is linked to obesity independent of other comorbidities [64, 71].

A systematic review and meta-analysis by Upala and colleagues evaluated 15 observational studies assessing the effect of bariatric surgery on patients with diabetic nephropathy. The results from this meta-analysis revealed a significant reduction in UACR (−6.6 mg/g of creatinine) and a reduction in albuminuria (−55.76 mg in 24 h) after bariatric surgery with short-term follow-up [72].

Young and colleagues retrospectively evaluated the long-term changes of UACR in 101 patients with preoperative diabetes and albuminuria. The median UACR decreased from 80 mg/g prior to surgery to 30 mg/g at last follow-up (61 months). Along with significant weight reduction and glycemic control, albuminuria resolved in 77% of these patients and improved in 51% [73].

The STAMPEDE trial reported its 5-year renal outcomes. There was a significant decrease in UACR only in the sleeve gastrectomy group compared to medical

therapy. There was a significant decrease in both creatinine and GFR from baseline among participants in the RYGB and SG cohorts, not demonstrated in the medical therapy cohort. There was no significant change in albuminuria status at 5 years between the three treatment groups, although, more participants in the surgical groups had albuminuria at baseline that resolved by 5-year follow-up [57].

To assess whether remission of diabetes is related to improvement in eGFR, proteinuria, and risk for CKD, Friedman et al. performed a large, multicenter, prospective cohort study of over 700 bariatric surgery participants (from the Longitudinal Assessment of Bariatric Surgery-2 study) with T2D with 5-year follow-up. This study found that partial or complete remission of diabetes was associated with improvement in albuminuria and stabilization of CKD risk. There was negligible change in eGFR, however, even after excluding those with hyperfiltration. A higher baseline eGFR was associated with increased odds of diabetes remission, while this association was not found for baseline UACR [74].

Using glomerular filtration rates to measure the effect of bariatric surgery on kidney function can be less reliable than UACR due to significant variation in GFR values due to obesity-related hyperfiltration [75]. A large, retrospective, matched-cohort study from Kaiser Permanente Southern California's patient registry evaluated patients with CKD, stages 3 and 4, before and after bariatric surgery ($n = 714$) and compared them to a group of nonsurgical controls ($n = 714$). The primary endpoint was change in eGFR over a median 3-year follow-up period. There was a significant increase in eGFR in surgery patients compared to controls (9.84 mL/min/1.73 m^2 greater) and also in those undergoing RYGB compared to SG (6.60 mL/min/1.73 m^2 greater) [76].

MicroRNAs (miR) are endogenous RNAs that regulate gene expression through silencing the translation of mRNAs. They have emerged as a viable biomarker in several disease states due to their stability in biofluids and simple detectability through PCR and other platforms. At the urinary level, miRNAs have been detected in immunoglobulin A nephropathy and bladder cancer. A longitudinal, prospective study of 24 bariatric surgery patients (compared to obese and healthy controls) revealed that miR 192, mi200a, and mi200b were upregulated in urine following bariatric surgery with a profile reflecting controls with obesity preoperatively to healthy controls over 100 days postoperatively. Obesity and diabetes share a similar mechanism in the development of CKD through epithelial-to-mesenchymal transition (EMT). MicroRNAs 192 and those in the 200 family inhibit EMT by down-regulating ZEB1 and ZEB2 and consequently decreasing collagen deposition in the extracellular matrix [77]. Continuing research into reliable markers to measure kidney function will further establish metabolic surgery's impact on renal function.

10.8 Conclusions

There is mounting evidence that metabolic and bariatric surgery has a beneficial impact on renal function for at-risk patients with obesity and metabolic disease. Risk of postoperative complications such as acute kidney injury and nephrolithiasis may be higher in those with baseline renal dysfunction, however, metabolic surgery

remains a safe option for this population. Furthermore, long-term evidence is favorable for metabolic surgery reducing the risk of microvascular complications from obesity and diabetes. Select patients awaiting transplantation may also benefit from metabolic surgery to reduce waiting times and reduce the relative contraindications related to obesity. Several markers are available to assess and follow renal function in and beyond the perioperative period to monitor at-risk patients and their response to surgery. The high-risk patients with pre-existing advanced CKD, multiple comorbidities, and advanced age are at risk for developing renal dysfunction and must be monitored closely.

Key Points

1. *Mechanisms by which obesity leads to renal dysfunction include obesity-mediated hypertension, insulin resistance, glomerular hypertrophy, activation of the renin–angiotensin–aldosterone system, inflammation, and adipocytokine dysregulation.*
2. *Obesity affects the kidney through a process known as obesity-related glomerulopathy.*
3. *The most common clinical manifestation of obesity-related renal disease is proteinuria.*
4. *Appropriate management of postoperative AKI in the bariatric and metabolic surgery population involves early identification of renal dysfunction, aggressive hydration with intravenous fluids for prerenal causes such as dehydration, bleeding, and hypovolemia from sepsis.*
5. *De novo kidney stone formation after RYGB in those with no prior stone history ranges from 3 to 8%.*
6. *Metabolic and bariatric surgery is safe in select patients with CKD and should not be perceived as a contraindication for surgery.*
7. *There is a slightly higher risk for early postoperative complications in patients with CKD but long-term evidence shows a benefit in overall renal function.*
8. *Bariatric surgery serves as an effective bridge to transplantation for ESRD patients who are unable to be listed due to class III or higher obesity, and this is a more reliable weight loss strategy than nonoperative management.*
9. *Remission or mitigation of obesity-related comorbidities through metabolic surgery can improve outcomes for renal transplant recipients.*
10. *Metabolic surgery reduces the risk of CKD, stage 3 or higher, from progressing to kidney failure.*

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