Review Article Kidney360

# Risk Factors for Kidney Stone Formation following Bariatric Surgery

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# **Abstract**

Kidney stones are painful, common, and increasing in incidence. Obesity and bariatric surgery rates are also on the rise in the United States. Although bariatric surgery is associated with improvements in metabolic outcomes, malabsorptive bariatric surgery procedures are also associated with increased risk of kidney stones. Restrictive bariatric surgeries have not been associated with kidney-stone risk. Higher risk of kidney stones after malabsorptive procedures is associated with postsurgical changes in urine composition, including high urine oxalate, low urine citrate, and low urine volume. Certain dietary recommendations after surgery may help mitigate these urine changes and reduce risk of kidney stones. Understanding risk of kidney stones after surgery is essential to improving patient outcomes after bariatric surgery.

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## Introduction

Kidney stones are a major cause of morbidity in the United States (1–4). The lifetime prevalence is estimated at 9% and expected to rise (5). Kidney stones are associated with acute pain and chronic conditions, such as bone disease (6,7), CKD (8,9), hypertension (10,11), and coronary heart disease (12,13). Prevention of kidney stones is critical to improving patient outcomes. Clinical prevention of kidney stones focuses on modifying risk factors for kidney stone formation. Obesity and certain bariatric surgeries are important clinical risk factors for kidney stones, particularly given that rates of both are on the rise in the United States (14–16). This review will discuss the risk of kidney stones after bariatric surgery and recommendations for mitigating that risk.

## **Obesity and Bariatric Surgery**

Obesity and metabolic syndrome are wellestablished risk factors for kidney stones. Higher body mass index (BMI), larger body size, and weight gain are each strongly associated with higher risk of kidney stones in men and women (17,18). For example, compared with a BMI of 21–22.9 kg/m², the multivariate relative risk for developing kidney stones with a BMI of ≥30 kg/m² is 2.09 in young women, 1.90 in older women, and 1.33 in men (18). Furthermore, diabetes mellitus (19) and hypertension (20) are both independently associated with higher risk of developing kidney stones.

Bariatric surgery is a surgical option for the management of morbid obesity. Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) are currently the most common bariatric surgical procedures in the United States, making up nearly 80% of the 252,000 bariatric surgeries in 2018 (Figure 1) (21). Other

procedures that were previously popular, such as adjustable gastric band and biliopancreatic diversion with duodenal switch, are now less common and account for <2% of procedures (Figure 1) (21). RYGB and SG are also the two most common procedures performed outside of the United States, but there is some variability between rates of RYGB versus SG (22). For example, RYGB makes up 84% of bariatric surgeries in Canada, whereas SG makes up 100% of bariatric surgeries in Australia (22). In general, bariatric surgery is much more common in women, with female patients accounting for nearly 80% of all bariatric surgery procedures (15,22,23). RYGB is both a restrictive and malabsorptive procedure involving the creation of a small, proximal, stomach pouch that connects to a more distal part of the small intestine (24). SG is a purely restrictive procedure with the creation of a small stomach pouch (24). RYGB and SG are highly effective in management of morbid obesity, with significant weight loss and improvement in metabolic syndrome and cardiovascular outcomes (25-28).

# **Bariatric Surgery and Kidney-Stone Risk**

Despite the many positive metabolic outcomes, RYGB is also associated with higher risk of kidney stones (29–33) and bone disease (34–38) after surgery. Three years after surgery, new kidney stone incidence is 8% (30), and this continues to rise to 14% (32) 10 years after surgery. In comparison, the rate for kidney stones in controls with obesity is 5% and 7% at 3 and 10 years, respectively (30,32). Similarly, the multivariate hazards ratio of developing a kidney stone is 2.3 for patients who have had RYGB compared with controls with obesity (32). In contrast, restrictive procedures, including SG, have not been associated with risk of kidney stones or fracture (32). Given that SG has increased in

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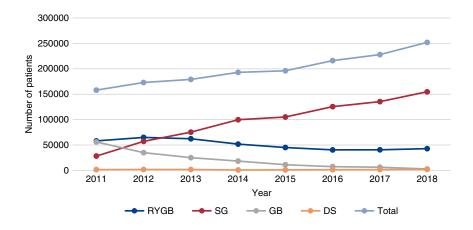


Figure 1. | Trend in more overall bariatric surgery procedures and more sleeve gastrectomies over time in the United States. DS, duodenal switch; GB gastric band; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy. Data from https://asmbs.org/resources/estimate-of-bariatricsurgery-numbers.

popularity only in the past few years, most studies of restrictive procedures and kidney stones have primarily included patients with adjustable gastric bands (31,39). One study that examined incidence rates in 85 patients with an SG found that only 1% of patients with an SG developed a stone after a mean of just over 2 years of follow-up (40). A recent, retrospective review found that 8% of patients who underwent RYGB surgery compared with 4% of patients with an SG (P<0.001) developed a kidney stone postoperatively, with a mean follow-up of nearly 3 years (41). However, additional studies of patients who have undergone an SG with longer followup time are needed to better characterize the overall stone risk associated with SG.

# **Kidney Stone Type and Urine Composition Changes** after RYGB Surgery

Calcium oxalate stones are the most common stone type reported after RYGB (29,32,42). Prior studies have found that mean 24-hour urine calcium oxalate supersaturation (CaOx SS) increases post-RYGB (42-44). Similarly, one study found that individuals who form kidney stones after RYGB had higher 24-hour urine CaOx SS compared with those who did not form kidney stones after RYGB (32). These findings are consistent with data in patients without bariatric surgery that show higher urine CaOx SS is associated with higher risk of being a kidney-stone former (45). For this reason, understanding postsurgical changes in urine CaOx SS and its major contributors can provide insight into why some individuals form kidney stones after surgery. The primary individual urine components that influence urine CaOx SS level include urine calcium, oxalate, citrate, and volume (46). High levels of urine calcium or oxalate, or low levels of urine volume or citrate, each individually increase urine CaOx SS and kidney stone risk (46–48). After surgery, patients who have undergone RYGB surgery may experience changes in one or more of these urine components which leads to higher urine CaOx SS. Common alterations in urine composition seen after surgery include high urine oxalate, low urine volume, and low urine citrate.

# Hyperoxaluria

High urine oxalate is one of the most prominent factors associated with higher CaOx SS and, thus, higher kidneystone risk after malabsorptive bariatric surgery. This is unique to the malabsorptive procedures, such as RYGB, because the restrictive procedures have not been associated with high urine oxalate (31,39). Multiple studies have demonstrated that mean urine-oxalate levels rise significantly after RYGB when preoperative oxalate excretion was compared with postoperative oxalate excretion 6-12 months after surgery (Table 1) (39,42-44,49-57). For example, in a study of 151 patients who underwent RYGB surgery, Valezi et al. (53) found that urine oxalate increased from 24 mg/d pre-RYGB to 41 mg/d 12 months post-RYGB. In addition, some (56), but not all (58), studies in which patients with obesity were compared with patients who had undergone RYGB showed higher urine oxalate in the patients who had undergone surgery. In one cross-sectional study, 19 patients who had undergone RYGB surgery had a mean urine oxalate of 45 mg/d, compared with 30 mg/d in controls with obesity (56). Notably, both of these levels are well above the level of urine oxalate at which risk of kidney stones begins to rise (20-25 mg/d) (47). Frank hyperoxaluria, levels of oxalate above the normal range, occur in a significant number of patients after RYGB, which has been estimated at 42%-67% after at least 6 months of follow-up (50,55,56). In contrast, a recent study by Moreland et al. (57) found no difference in mean urine-oxalate levels in patients before versus after RYGB (61 versus 69 mg/d; P=0.92). However, given that urine-oxalate levels were very high both before and after surgery, high urine-oxalate levels were still an important finding in that study and a contributor to kidney-stone risk in those patients.

The high urinary oxalate pre-RYGB is likely related to the association between obesity and hyperoxaluria. Hyperoxaluria in obesity is thought to be secondary to inflammation causing increased oxalate absorption in the gut (59,60). High urine oxalate after a malabsorptive bariatric surgery is described as enteric hyperoxaluria. Enteric hyperoxaluria is the process of enhanced gut absorption of dietary oxalate that occurs in the setting of fat malabsorption (52,61,62). In

Table 1. Changes in 24-hour urine parameters in prospective studies of patients who have undergone bariatric surgery

Study	Procedure	N	Time to FU (mo)	Sex (n M/F)	CaOx SS	Oxalate	Calcium	Citrate	Volume
Park <i>et al.</i> (50)	RYGB	45	6–12	8/37	1	1	<b>↓</b>	<b>↓</b>	<b>↓</b>
Duffey et al. (55)	RYGB	21	24	5/16	No change	1	$\downarrow$	1	No change
Kumar et al. (52)	RYGB/ BPD	11	12	0/11	1	No change	No change	No change	No change
Wu et al. (54)	RYGB	38	6	7/31	1	1	1	No change	<b>1</b>
Valezi et al. (53)	RYGB	151	12	42/109	Not reported	1	$\downarrow$	↓ °	$\downarrow$
Agrawal et al. (43)	RYGB	13	6	2/11	1	1	No change	$\downarrow$	No change
Moreland <i>et al.</i> (57)	RYGB	26	12	9/17	No change	No change	Not reported	Not reported	Not reported

Patients were studied before bariatric surgery and at the specified time point postoperatively. Most patients were nonstone formers. FU, follow-up; M, male; F, female; CaOx SS, calcium oxalate supersaturation; RYGB, Roux-en-y gastric bypass; BPD, biliopancreatic diversion with duodenal switch.

the postsurgical gut, higher levels of free fatty acids bind to dietary calcium. This lowers the amount of calcium available in the gut to precipitate with dietary oxalate and leads to higher levels of unbound oxalate in the gut. This unbound oxalate is more likely to be absorbed by the gut. Additionally, higher levels of bile salts and fatty acids increase the permeability of oxalate in the colon (63). As a result, more oxalate is absorbed in the colon (64) and this oxalate is eventually excreted in the urine. Urine-oxalate levels begin to increase within months of surgery (42,43,51) and may remain high for years after surgery (39).

# **Urine Volume and Citrate**

Low urine volume (43,53,54) and citrate (50,53,55,56) excretion are two other urine-composition changes that have been described after RYGB, although less consistently than increased oxalate, and both are important to understanding kidney -tone risk in this population (Table 1) (32,49,50). For example, Agrawal et al. (43) studied 13 patients from pre- to post-RYGB and found that, in addition to increased urine oxalate, urine volume decreased from 2.1 L to 1.4 L and urine citrate decreased from 540 mg/d to 305 mg/d. Other studies have found that the citrate is lower postoperatively in malabsorptive procedures compared with restrictive procedures. Penniston et al. (39) collected urine in patients with a gastric band and those with an RYGB for 3 years after surgery and found much lower urine citrate in patients with the RYGB compared with those with a gastric band. In the Penniston et al. study, both groups had low urine volume (39). Both Lieske et al. (32) and Valezi et al. (53) found that urine citrate was lower in those patients who formed stones after RYGB compared with those that did not. The etiology for low urine volume may be partially related to low fluid intake due to the restrictive nature of the procedure. Low urine volume may also be related to water losses in stool because diarrhea is common after RYGB (65), and may be more common in RYGB compared with SG (66). To our knowledge, this has not been more fully studied in the context of kidney-stone risk. Low urine citrate may be related to metabolic acidosis, as seen in other states of acid

retention (67,68). Two studies that reported urine ammonia excretion found that it was higher after RYGB compared with either controls with obesity or normal subjects, suggesting increased acid excretion (51,56). Additional study is needed to better understand why urine volume and citrate levels are low in patients who have undergone bariatric surgery.

# **Diet and Supplements**

Diet, including specific food choices and certain diet patterns, is a well-established risk factor for kidney stones in individuals who have not had bariatric surgery. For example, diets low in fruits and vegetables are associated with low urine citrate (69), and diets high in oxalate are associated with high urine oxalate (70). A low-calcium diet is associated with higher kidney stone recurrence compared with a normal-calcium, low-salt diet (71). The Dietary Approaches to Stop Hypertension diet pattern has been associated with lower kidney-stone risk (69). Low dietary fluid intake associates with low urine volume (72) and, thus, to higher risk of being a stone former (47).

Due to postsurgical anatomy, patients who have undergone bariatric surgery have unique dietary limitations and nutritional and supplemental requirements. Such patients receive dietician guidance before and after surgery. However, adherence to diet recommendations is poor both before and after surgery (73,74). There has been very limited study of diet and kidney-stone risk in patients who have undergone bariatric surgery. In one small study of diet in patients after RYGB surgery, Pang et al. (75) measured 24hour urine in six patients after RYGB surgery who were on an individual home diet and after 4 days on a controlled diet. The controlled diet contained limited oxalate (70-80 mg/d), the recommended daily amount of calcium (1000 mg), and moderate sodium. The investigators found urinary oxalate did not statistically change from home diet to controlled diet. Interestingly, they did find that CaOx SS was lower on the controlled diet, despite the lack of statistical difference in urine oxalate, volume, citrate, or calcium on the home versus controlled diet (75). This may highlight the concept that a multimodal approach is key to managing kidney-stone risk in this patient population. Other studies have found that limiting dietary oxalate in patients after bariatric surgery is important for urine-oxalate levels. Froeder et al. (58) gave study participants an oral oxalate load and measured urine-oxalate levels for 6 hours. The urine-oxalate levels peaked 4 hours after the oral load and were higher in patients postsurgery compared with both patients who were presurgery and those with obesity (58). This demonstrates that, due to enteric hyperoxaluria, patients absorb more of their dietary oxalate after RYGB surgery.

There have not been larger studies in patients with an RYGB reviewing home versus controlled diets to further guide dietary recommendations for reducing kidney-stone risk. To our knowledge, there are no studies guiding a recommended daily intake for oxalate in the bariatric surgery patient population. Most experts on kidney stones agree that common dietary guidance should include recommendations to avoid high-oxalate foods. One good source for oxalate content of individual foods can be found at https:// regepi.bwh.harvard.edu/health/Oxalate/files. This source provides lists of high- and low-oxalate-content foods and can help guide patients when making food choices with the goal to reduce hyperoxaluria. Patients should also consume at least the daily recommended amount of dietary calcium after bariatric surgery. An additional recommendation to reduce hyperoxaluria is to time calcium supplement intake with food. This has not been demonstrated to be effective in patients who have undergone bariatric surgery but, in nonbariatric patient populations, this strategy is often used to reduce urine-oxalate levels. Adequate dietary calcium and taking supplemental calcium with food may lower urineoxalate levels because the calcium binds with dietary oxalate in the gut and the oxalate-calcium complex is unabsorbed and excreted by the gut (76-78). Some providers have also recommended reducing dietary fat intake to reduce fatty acids in the gut and the effect of enteric hyperoxaluria. To our knowledge, this has not been formally studied in modern RYGB procedures but has been shown to be effective in early malabsorptive procedures, such as jejunoileal bypass (79,80). Other dietary recommendations for reducing kidney stones in patients who have had bariatric surgery include increasing fluid intake to increase urinary volume. This recommendation should be attempted, while keeping in mind that a restricted stomach size may make this difficult to achieve. It is often recommended to consume fluids between meals instead of with the meal. In addition, a citrate-rich diet (fruits and vegetables) and consideration of use of citrate supplementation (often prescribed as potassium citrate) may increase urine citrate and reduce overall kidney-stone risk (33,81,82). Finally, study of potassium calcium citrate, an effervescent form of calcium and alkali supplementation, has been shown to increase urine citrate and decrease bone resorption after RYGB and, thus, may be a therapeutic option for these patients (83,84).

# **Conclusions**

Bariatric surgery is effective at treating obesity and metabolic syndrome, but certain procedures, notably RYGB, are associated with increased calcium oxalate kidney-stone risk. Higher kidney-stone risk after RYGB is related to high CaOx SS from high urine oxalate, low urine citrate, and low urine volume. Restrictive bariatric surgery procedures have not been associated with the same alterations in urine composition or kidney-stone risk. Clinical management to reduce risk of kidney stones is focused on dietary modifications, although dietary studies in this population have been limited. Common recommendations include a low-oxalate diet, timing calcium supplementation with meals, increased fluid intake, and possible citrate supplementation. As obesity, metabolic syndrome, and bariatric surgery rates continue to rise, these strategies will be crucial for reducing kidneystone risk and improving outcomes in patients who undergo bariatric surgery.

#### **Disclosures**

E. Worcester reports being a member of the Kidney Health Initiative Enteric Hyperoxaluria group and receiving personal fees from Allena, Alnylam, Bridgebio Pharmaceutical, Dicerna, and OxThera, outside the submitted work. The remaining author has nothing to disclose.

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#### **Author Contributions**

M. Prochaska conceptualized the study and wrote the original draft; E. Worcester provided supervision and reviewed and edited the manuscript.

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