International Journal of Surgery 36 (2016) 618–623

Contents lists available at ScienceDirect

International Journal of Surgery

journal homepage: www.journal-surgery.net

Review

# Nephrolithiasis after bariatric surgery: A review of pathophysiologic mechanisms and procedural risk

Umer Hasan Bhatti [a], Andrew J. Duffy [b], Kurt Eric Roberts [b], Amir Hafeez Shariff [a, *]

[a] Aga Khan University Hospital, Department of Surgery, Stadium Road, P. O. Box 3500, Karachi, 74800, Pakistan
[b] Yale University School of Medicine, Department of Surgery, 40 Temple Street, Suite 7B, New Haven, CT, 06510, USA

## HIGHLIGHTS

- Both obesity and bariatric surgery are associated with an increased risk for nephrolithiasis.
- Stone formation risk varies with the type of bariatric surgical procedure.
- Increased calcium oxalate saturation, hypocitraturia and decreased urinary volume contribute to stone formation.
- Nephrolithiasis post bariatric surgery is typically managed medically.

## ARTICLE INFO

*Article history:*
Received 18 October 2016
Accepted 10 November 2016
Available online 12 November 2016

*Keywords:*
Bariatric surgery
Nephrolithiasis
Enteric hyperoxaluria
Complications
Malabsorptive procedures
Restrictive procedures

## ABSTRACT

Obesity alone is a known risk factor for nephrolithiasis, and bariatric surgery has been linked to a higher incidence of post-operative new-onset nephrolithiasis. The mean interval from bariatric surgery to diagnosis of nephrolithiasis, ranges from 1.5 to 3.6 years.

The stone risk is greatest for purely malabsorptive procedures, intermediate for Roux-en-Y gastric bypass and lowest for purely restrictive procedures (laparoscopic adjustable gastric banding, laparoscopic sleeve gastrectomy) where it approaches or is reduced below that of non-operative obese controls. A history of nephrolithiasis and increasing age at the time of surgery are both associated with an increased risk of new stone formation post-operatively.

The underlying pathophysiologic changes following bariatric surgery include increased colonic absorption of oxalate leading to hyperoxaluria, hypocitraturia and increased urinary calcium oxalate supersaturation, which predispose to stone formation. The majority of incident stones are medically managed, with some requiring interventions in the form of lithotripsy or ureteroscopy.



## 1. Introduction

With more than one third of the adult population obese (Body Mass Index (BMI) ≥30 kg/m$^2$), morbidly obese (grade 3 obesity, BMI ≥40 kg/m$^2$) individuals accounted for 6.4% of the adult U.S. population in 2011–2012 [1], though this increasing prevalence has plateaued over the last decade [1]. Globally, the proportion of adults with a body mass index (BMI) of 25 or greater has increased from 28.8% in 1980 to 36.9% in 2013 for men and from 29.8% to 38.0% for women with increases observed in both developed and developing countries. Of concern is the finding that in some countries the estimated prevalence of obesity exceeds 50% [2].

Obesity has become a major global health challenge. In addition to lifestyle modifications and because of the limited efficacy of pharmacotherapy, bariatric surgery remains an important option for management of the morbidly obese. Recent large randomized controlled trials have shown bariatric surgery to lead to sustained weight loss, decreased mortality and a decrease in obesity-related complications such as diabetes, hypertension and obstructive sleep apnea [3,4].

### 1.1. Procedures

About 196,000 bariatric procedures were performed in the US in 2015, based on American Society for Metabolic and Bariatric Surgery (ASMBS) estimates [5] (from BOLD, ASC/MBSAQIP and the National Inpatient Sample). The most commonly performed bariatric procedures were laparoscopic sleeve gastrectomy (LSG)

* Corresponding author.
*E-mail address:* amir.shariff@aku.edu (A.H. Shariff).

http://dx.doi.org/10.1016/j.ijsu.2016.11.025
1743-9191/

(53.8%) and laparoscopic Roux-en-Y gastric bypass (RYGB) (23.1%), with the remainder being laparoscopic adjustable gastric banding (LAGB) (5.7%) and malabsorptive procedures (0.6%, Biliopancreatic Diversion (BPD) and Duodenal Switch (DS)). LSG in particular has shown rapid adoption [6,7].

International surveys [8] by members of the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) estimate worldwide bariatric procedures reached 468,609 in 2013, 95.7% of these laparoscopic. The most commonly performed procedure was the RYGB, 45%; followed by sleeve gastrectomy (SG), 37%; and adjustable gastric banding (AGB), 10%. SG rose from 0 to 37% of the world total between 2003 and 2013, while AGB declined from its peak of 68% in 2008–2013.

### 1.2. The risk of nephrolithiasis

Obesity alone is a known risk factor for nephrolithiasis and chronic kidney disease, however, once BMI is > 30 kg/m$^2$, further increases in BMI do not significantly increase the risk of renal stone disease [9]. Prospective studies on obese patients have identified diabetes, osteoarthritis, obstructive sleep apnea and being a candidate for bariatric surgery as significant risk factors for the development of nephrolithiasis [10].

Bariatric surgery has long been linked to a higher incidence of new-onset nephrolithiasis, with the mean interval from surgery to diagnosis of nephrolithiasis ranging from 1.5 to 3.6 years [11–13]. The risk of nephrolithiasis varies by procedure, being the highest for malabsorptive procedures (22–28.7% [10,14]), intermediate for RYGB (7.65–13% [10,13,15]) and the lowest for purely restrictive procedures (LAGB, LSG) where it approaches that of non-operative obese controls [10,16].

Those with a history of a prior stone at the time of bariatric surgery are more likely to form a stone after surgery than those without a prior stone history (42% vs 14% at 10 years; HR = 4.1, $p < 0.001$) [10]. However, the risk of prevalent obese patients forming a second stone is higher (31.4–52%) [10,13], reflecting the known tendency for stone event risk to increase as the number of prior events increases [17]. Additionally, while the percentages above reflect the incidence of nephrolithiasis in all post-bariatric surgery patients, amongst patients with no prior history of stones, the incidence of *de novo* stone formation after RYGB has been reported between 3.1 and 7.7% [13,18].

## 2. Review

### 2.1. Pathophysiology

The underlying pathophysiology of nephrolithiasis following bariatric surgery is complex and several mechanisms have been described, including hyperoxaluria, hypocitraturia, and aciduria, as increasing the risk of stone formation. Additionally, the supersaturation of urine by calcium and oxalate is essential for the formation of calcium oxalate crystals, and later, stones [19,20].

#### 2.1.1. Hyperoxaluria

Oxalate is an endogenous byproduct of amino acid metabolism and is also absorbed by the stomach, small bowel and colon [21]. Typically, all oxalate absorbed from the diet or produced endogenously is excreted unchanged in urine. Normal urinary oxalate excretion varies but a value above 40–45 mg/day (0.45 mmol) is considered abnormal and labeled hyperoxaluria.

Enteric hyperoxaluria is a form of secondary hyperoxaluria, caused by increased intestinal absorption of oxalate due to malabsorption syndromes. This is thought to be secondary to an increase in oxalate solubility in the intestinal lumen and a concurrent rise in mucosal permeability to oxalate, due to bile salts and mucosal inflammation as seen in IBD [22]. Normally, dietary calcium binds dietary oxalate and precipitates out as calcium oxalate to be excreted in stool. In enteric hyperoxaluria, non-absorbed fatty acids preferentially bind calcium in the small intestine, rendering it unavailable to precipitate oxalate. Soluble oxalate is consequently present in relatively high concentrations in the colon and can diffuse passively into blood, where it is filtered and excreted by the kidneys [21]. The study by Modigliani and colleagues [23] was particularly interesting for one additional experimental finding: direct intracolonic perfusion of calcium abolished or greatly reduced the hyperoxaluria in the presence of constant fat content, a finding supported by later studies demonstrating decreased gastrointestinal absorption and urinary excretion of oxalate in patients placed on a high calcium diet (3000 mg/day) [24,25].

Hyperoxaluria, first described in patients undergoing the jejunoileal bypass (JIB) (see below), has been reported in almost two thirds of patients who have undergone RYGB [11,12,26–29]. The onset is seen as early as 1 year after surgery [11,27], and studies report no significant difference after 1- and 2-years postoperatively [27]. Mean baseline 24-h urinary oxalate concentrations typically increase 2–3 times [10,11,27] postoperatively, and are affected by the patient's dietary intake and health status. However, urinary oxalate in the Rochester Epidemiology Project cohort [10] was shown to increase in all patients following RYGB, but with a more significant increase in those who developed kidney stones with concurrent calcium oxalate supersaturation being highest in those patients who developed kidney stones. *Therefore, the incidence of calcium oxalate stones following bariatric surgery increases, whereas the incidence of other (hydroxyapatite, struvite, uric acid) stone compositions does not change*. Additionally, in a multivariate analysis, increasing age at the time of surgery was the only *baseline* characteristic predicting the onset of *de novo* hyperoxaluria [27].

Increased fecal fat content has been shown in only one study [30] of 11 patients following RYGB, where intestinal fat malabsorption was linked with the rise of plasma oxalate and thereby significantly elevated urinary calcium oxalate supersaturation. The authors therefore suggested that complex formation of unabsorbed fatty acids with calcium and/or magnesium in the intestinal lumen increases intestinal oxalate content and absorption, which was later confirmed with oral oxalate loading following bariatric surgery, showing an increase in urinary oxalate excretion 2–4 h after oxalate load [31,32].

Secondly, a number of bacterial species are known to degrade luminal oxalate, chief among these *Oxalobacter formigenes*, a Gram-negative anaerobe and commensal organism present in the colon. The association between colonization by *O. formigenes* has been found to confer a protective effect against stone formation (OR 0.3, 95%CI 0.1–0.7) [33]. Alterations in intestinal microbial flora following bariatric surgery potentially modify ileocolic colonization of *O. formigenes*, leading to further increased oxalate absorption.

In addition to the gut eliminating excess oxalate in conditions of chronic kidney disease, when enteric elimination of oxalate is promoted, urinary oxalate can be reduced even in hyperoxaluric conditions [34].

#### 2.1.2. Hypocitraturia

Hypocitraturia following RYGB is common, but less so than hyperoxaluria [11,12,27–29], with a prevalence varying from 24 to 63% [27,29,31,35]. Citrate is the dissociated anion of citric acid, a weak acid ingested in dietary fruits and vegetables and produced endogenously via the tricarboxylic acid cycle. Acid-base status is critical in citrate excretion. Acidosis leads to increased mitochondrial citrate utilization, thus increasing renal citrate reabsorption and decreasing excretion in urine [36]. Assuming a 2-L urine output