ELSEVIER

Surgery for Obesity and Related Diseases ▮ (2014) 00–00

SURGERY FOR OBESITY AND RELATED DISEASES

Review article

Kidney stone incidence and metabolic urinary changes after modern bariatric surgery: review of clinical studies, experimental models, and prevention strategies

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Received January 14, 2014; accepted March 8, 2014

Keywords: Morbid obesity; Gastric bypass surgery; Nephrolithiasis; Kidney stone; Calcium oxalate supersaturation; Hyperoxaluria; Hypocitraturia; Metabolic acidosis

Obesity in the United States is an overwhelming clinical problem, with recent estimates suggesting over a third of American adults are obese (body mass index [BMI] >30 kg/m^2), including >15 million who are considered morbidly obese (BMI >40 kg/m^2) [1–3]. For these patients, medical weight loss tends to be either temporary or completely ineffective. To date, bariatric surgery is the most effective means of long-term weight loss, curing obesity-related diabetes and hypertension as well as lowering cardiovascular and overall mortality risk in this population [4,5]. These successes have led to a 6-fold increase in bariatric surgery in the United States over the last 10 years, from 36,700 procedures in year 2000 to 220,000 procedures in year 2009 [4,6].

In 2005, Nelson et al. [7] first described the renal complications of hyperoxaluria, calcium oxalate stones, and oxalate nephropathy in a select group of 23 patients after Roux-en-Y gastric bypass (RYGB) surgery. Since that report, >30 different publications have attempted to examine the potential metabolic derangements that raise kidney stone risk after bariatric surgery. In this review, published data detailing urinary chemistry profiles and kidney stone incidence after bariatric surgery are tabulated and summarized. Recent experimental data from human and animal studies that offer insight into the pathophysiology of stone risk will be critically examined, and a summary of recommendations that may reduce kidney stone risk in bariatric, stone-forming patients will be provided.

Literature review methods

Published studies were searched from electronic databases including Cochrane Central Register of Controlled Trials (The Cochrane Library), MEDLINE, and EMBASE. Reference lists were also made from bariatric surgery and urology textbooks as well as review articles. The search terms included all forms and abbreviations of nephrolithiasis, kidney stone formation, calcium oxalate supersaturation, and hyperoxaluria in regard to restrictive bariatric procedures, laparoscopic adjustable gastric banding (LAGB) and sleeve gastrectomy (SG), and malabsorptive bariatric procedures, biliopancreatic diversion with duodenal switch (BPD) and RYGB surgery. With the assumption that the reader is familiar with the technical nuances of each of these procedures, detailed differences among them will not be included in this review. Of the 31 clinical articles identified, 8 were excluded due to being case reports or bariatric case series containing <8 patients. The remaining studies containing pertinent clinical stone incidence and urine profiling ($n = 24$) or basic science experimentation were reviewed and summarized either in tables or within text. Although no data exists in the bariatric surgery arena, a brief review of enteric oxalate transporters is included within the basic science section of the text.

This study was supported by NIH K08 DK089000-04, AUA Foundation Rising Star in Urology Research Award, Astellas Global Development, Inc., and Ethicon Endo-Surgery.

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http://dx.doi.org/10.1016/j.soard.2014.03.026
1550-7289/Published by Elsevier Inc. on behalf of American Society for Metabolic and Bariatric Surgery.

Urinary chemistry profiles after bariatric surgery

Prospectively collected, 24-hour urine chemistry profiles from primarily nonstone formers before and after either RYGB or BPD procedure are summarized in Table 1 and detailed in supplemental Table S1. No studies with this stringent prospective design were identified in LAGB or SG patients. At a mean of 11 months post-RYGB, 277 patients were identified to have, on average, increased urinary oxalate levels from mean 28 mg/d to 44 mg/d on home diets (Table 1). Urine calcium oxalate supersaturation (CaOx SS), a calculated predictor of kidney stone risk that should be <2, increased from baseline of 1.5 to 2.3 postoperatively. In addition to increased urinary oxalate excretion and CaOx SS, Park et al. [8] also noted RYGB patients had decreased urinary citrate and total urine volume compared with their preoperative urine samples. Citrate, a potent endogenous inhibitor of calcium oxalate stone formation, can reduce CaOx SS by forming soluble complexes with calcium [9]. Although there were no symptomatic stone events after a mean of 9.6 study months in these patients, the authors of this study suggest that chronic acidosis may have led to decreased urinary citrate, further increasing stone risk [8].

Similarly, Duffey et al. [10] described a doubling of urinary oxalate excretion and significant decreases in urinary citrate excretion in a 2 year, prospective study in RYGB nonstone forming patients. Furthermore, their study importantly showed that risk of postoperative hyperoxaluria appears to increase over time, not decrease or remain stable [10]. To examine this hyperoxaluria phenomenon more closely, Kumar et al. [11] tested plasma and urinary oxalate, fecal fat excretion, and response to oral oxalate load in 9 pre- and post-RYGB and 2 pre- and post-BPD morbidly-obese patients. At 12 months postop, they found a 25% increase in urine oxalate, a 60% increase in plasma oxalate ($P = .016$), a 2-fold increase in calcium oxalate supersaturation ($P = .003$) and fecal fat excretion ($P = .26$), and a dramatic 50% increase in urine oxalate after oxalate load ($P < .02$) [11], suggesting that hyperabsorption of dietary oxalate from the gastrointestinal (GI) tract may increase stone risk (see enteric hyperoxaluria in Pathophysiology section).

Recently, 3 groups have described the temporal changes in CaOx SS in the early postoperative period after RYGB. Wu et al. [12] noted urinary changes 6 months after RYGB (n = 38) compared to baseline, including significant increases in urinary oxalate excretion, calcium, and CaOx SS (using the "relative supersaturation scale" from 5–10) and decreases in total urine volume. The lack of hypocitraturia and presence of hypercalciuria in this cohort, compared to previous studies, was judged to be due to increased utilization of calcium citrate supplementation in their patients postoperatively [12]. Agarwal et al. [13] evaluated 24 hour urines in 13 patients before and at time points 1, 2, 4, and 6 months after RYGB. Using a variety of standardized in-house assays and 1 private hospital-based laboratory, they noted a doubling of urinary oxalate starting at month 2–6 ($P = .005$), a 40% reduction in urinary citrate at month 6 ($P = .4$), and 30–60% reduction in urinary volume ($P < .001$) that started in the immediate postoperative month [13]. Lastly, Valezi et al. [14] studied the pre- to postoperative changes in urinary metabolites in 151 patients after RYGB, 16 of who had previous stone disease. At 1 year, urinary oxalate levels increased 37% (mean 24 mg/d to 41 mg/d, $P < .001$) while decreases in both urine citrate (36%; mean 268 mg/d to 170 mg/d, $P < .001$) and urine volume (29%; 1.3 liters/d to .9 liters/d, $P < .001$) were noted. Unlike Duffey et al. [10] who found that increasing age was a predictor for postoperative hyperoxaluria, this group found that presence of preoperative stones was the only predictor of hyperoxaluria [14]. Overall, across all 3 studies, RYGB increased CaOx SS 3–4 fold compared to patients' baseline studies, with over 80% of all patients having with CaOx SS >2.

Table 1
Summary of mean 24-hour urine data* and kidney stone incidence from obese controls, RYGB, or restrictive procedures stratified by stone history

RYGB and 24-hr urine (~12 mo F/U)	Patient number	Mean urinary oxalate	Mean urinary citrate	Mean urinary volume
Nonstone formers, prospective [8,10–14]	277	Preop = 28 mg/d Postop = 44 mg/d	Preop = 737 mg/d Postop = 442 mg/d	Preop = 1.6 L/d Postop = 1.1 L/d
Nonstone formers, retrospective [7,15,16,18,45,46]	177	54 mg/d	312 mg/d	1.1 L/d
Primarily stone formers, any type [17,44,47]	166	71 mg/d	415 mg/d	1.4 L/d
LAGB or SG and 24-hr urine				
Nonstone formers, retrospective [15,16]	30	36 mg/d	NR	1.3 L/d

Procedure, stone history (~2 yr F/U)	Kidney stone incidence
RYGB, stone history [14,21,52]	17/102 = 16.7%
RYGB, no stone history [14,21,22,52]	509/5955 = 8.5%
LAGB/SG, no stone history [24,25]	8/618 = 1.3%
Obese controls, no stone history [22,24]	227/4840 = 4.7%

F/U = follow-up; LAGB = laparoscopic adjustable gastric band; RYGB = Roux-en-Y gastric bypass; NR = not recorded; SG = sleeve gastrectomy
Primary data can be found in Supplemental data Tables S1–3.
*Mean values calculated using weighted averages from multiple studies.