Published in final edited form as:

Semin Nephrol. 2008 March ; 28(2): 163–173. doi:10.1016/j.semnephrol.2008.01.009.

Nephrolithiasis after bariatric surgery for obesity

John C. Lieske, M.D.^{1,2,4}, Rajiv Kumar, M.D.^{1,2,3,5}, and Maria L. Collazo-Clavell, M.D.^{1,3}

¹Department of Internal Medicine, Mayo Clinic College of Medicine Rochester, MN

²Division of Nephrology and Hypertension, Mayo Clinic College of Medicine Rochester, MN

³Division of Endocrinology, Diabetes, Metabolism and Nutrition, Mayo Clinic College of Medicine Rochester, MN

⁴Department of Laboratory Medicine and Pathology, Mayo Clinic College of Medicine Rochester, MN

⁵Department of Biochemistry and Molecular Biology, Mayo Clinic College of Medicine Rochester, MN

Abstract

Surgical intervention has become an accepted therapeutic alternative for the patient with medically complicated obesity. Multiple investigators have reported significant and sustained weight loss after bariatric surgery that is associated with improvement of many weight related medical co-morbidities, and statistically-significant decreased overall mortality for surgically-treated as compared to medically-treated subjects. Although the Roux-en-Y Gastric bypass (**RYGB**) is considered an acceptably safe treatment, an increasing number of patients are being recognized with nephrolithiasis after this, the most common bariatric surgery currently performed. The main risk factor appears to be hyperoxaluria, although low urine volume and citrate concentrations may contribute. The incidence of these urinary risk factors amongst the total post-RYGB population is unknown, but may be more than previously suspected based upon small pilot studies. The etiology of the hyperoxaluria is unknown, but may be related to subtle and seemingly sub clinical fat malabsorption. Clearly, further study is needed, especially to define better treatment options than the standard advice for a low fat, low oxalate diet, and use of calcium as an oxalate binder.

Keywords

bariatric surgery; enteric hyperoxaluria; nephrolithiasis; obesity; oxalate; Roux-en-Y gastric bypass

The Problem of Obesity

As much as 20% of the United States population is currently classified as obese (body mass index (BMI) > 30 kg/m²), including 11.5 million who are morbidly obese (BMI > 40 kg/m²) [1]. Of these, up to 5 million Americans have what is deemed medically-complicated obesity, since they have weight-related co-morbidities such as concurrent diabetes mellitus, hypertension, sleep apnea, or other severe weight-related conditions. Since diet and life style interventions have been disappointing for durable weight loss, increasing numbers of patients choose surgical interventions to treat their illness [2–7]. Indeed, most currently performed bariatric procedures result in marked and sustained weight loss, associated with improvements

Correspondence: John C. Lieske, M.D. Mayo Clinic Division of Nephrology and Hypertension 200 First Street SW Rochester, MN 55905
Telephone: (507)284-2064; FAX: (507)266-4710 Lieske.John@mayo.edu.

Conflicts of Interest: None

in abnormal glucose homeostasis, insulin resistance, sleep apnea, hypertension, and cardiovascular risk factors [8–13]. Of these, Roux-en-Y Gastric bypass (**RYGB**) procedures are most commonly performed in the U.S [5]. Two very recent studies confirm an overall benefit for weight loss and overall mortality amongst those that undergo bariatric surgery [14,15]. In 1991 an NIH conference deemed a BMI > 40 kg/m² an indication for bariatric surgery. Additionally, patients with a BMI > 35 kg/m² plus a weight related medical conditions such as diabetes were considered good candidates [16]. The recent trend has been to broaden these eligibility criteria even further to consider other less extreme co-morbidities such as obstructive sleep apnea and severe lymph edema when contemplating a surgical treatment [17].

Surgical Options for Obesity Treatment

The bariatric procedures currently employed promote weight loss via varied mechanisms (Figure 1). Restrictive procedures such as vertical banded gastroplasty (**VBG**) and laparoscopic adjustable gastric band (**LAGB**) each limit caloric intake by the physical restriction imposed by the band on dietary intake. The VBG consists of a stapled proximal gastric pouch with a fixed and non-adjustable outlet created by a mesh band or Silastic ring. Although still performed, poor long term outcomes for weight loss and maintenance have led many bariatric surgeons to abandon this procedure [7,18,19]. LAGB consists of two components, a silicone gastric band with an inner inflatable cuff and a reservoir connected by tubing. The band is placed around the gastric cardia to create a 15 mL proximal gastric pouch with an adjustable restrictive outlet connected to the reservoir implanted in the subcutaneous tissue of the abdominal wall. Access to the reservoir with the ability to add or remove saline allows modification of the dietary restriction imposed. [18,20] (Figure 1). The biliopancreatic diversion with the duodenal switch (**BPD-DS**) promotes weight loss by causing malabsorption of nutrients. The first portion of the duodenum is transected with resection of the greater curvature of the stomach, leaving a 100–150 mL lesser curvature-based gastric sleeve with an intact antrum and pylorus. The proximal ileum is divided 250 cm from the ileocecal junction, and the biliopancreatic limb is anastomosed to the distal ileum creating a short (100 cm) common channel. Then, duodenoileostomy anastomosis is made by bringing the Roux limb up to the gastric sleeve (Figure 1) [18].

By far, the most common bariatric surgery offered is the RYGB, a procedure that promotes weight loss by both dietary restrictions that result from the formation of a small (10–30 mL) gastric pouch, and maldigestion of nutrients from formation of a gastrojejunal anastomosis with a Roux limb promoting a “dumping” physiology. The length of the Roux limb can vary from 75 (“Proximal RYGB”) to longer than 200 cm (“Distal RYGB”). The longer the Roux limb, the greater the role of malabsorption of nutrients as a mechanism for weight loss (Figure 1) [18]. Since studies suggest that RYGB results in greater and more sustained long term weight loss with acceptable risks, it is currently the more widely performed procedure [21], although preferences and frequencies of various procedures are very center-specific.

Complications of Obesity Surgery

The current bariatric procedures have been deemed relatively safe and effective, even though both short-term and long-term complications have been recognized, including osteopenia, osteomalacia, and more rarely neurologic disorders [22–28]. Overall morbidity rates vary from 10–23% depending on the surgical procedure performed, although these have been declining due to increased attention to potential metabolic consequences (e.g., calcium and other micronutrient status) [8,29]. However, until very recently increased risk of nephrolithiasis was not considered a potential risk [31]. Mortality rates reported are less than 1% with the current procedures, although higher mortality rates have been reported amongst Medicare beneficiaries

[30]. Importantly, two recent studies strongly suggest long-term mortality benefits for recipients of both restrictive and gastric bypass procedures, compared to un-operated, control obese subjects [14,15].

Hyperoxaluria after JI Bypass: lessons from the past

Historically, nephrolithiasis was a well-recognized complication of bariatric surgery. In particular the development of calcium oxalate stones was a serious complication of jejunoileal (JI) bypass surgery performed in the 1970's for the management of obesity and hypercholesterolemia. This risk for nephrolithiasis, renal failure and other life threatening complications such as liver disease led to the abandonment of this operation more than 20-years ago [32].

The best evidence regarding the true risk of complications from this procedure comes from a single center report in the mid 1990's [33]. In this study, 453 patients were followed long term after JI bypass. The risk of renal complications increased linearly over 15 years to ultimately reach an incidence of nephrolithiasis of 28.7% and of renal insufficiency of 9.0%. These alarming data suggest that the risk of complications from modern RYGB may be cumulative as well, especially as years at risk begin to accumulate amongst the large number of patients those who have recently undergone this newer procedure. Even if the prevalence of hyperoxaluria, stones and renal damage is less than after JI bypass, the total number of cases could be substantial since only about 25,000 JI bypass procedures were completed in the US before the procedure was discontinued in the early 1980s, whereas 103,000 RYGB surgeries were completed in the US during 2003 alone [34]. A more recent study has confirmed that long-standing JI-bypass patients have marked hyperoxaluria, relative hypercalciuria, lowish urinary citrate levels, and normal volumes [35]. The net effect is a marked increase in calcium oxalate supersaturation, and the patients produce almost entirely calcium oxalate stones, a few of which contain a small percentage of uric acid [35].

The mechanisms of hyperoxaluria were relatively well-described during the 1970s and 1980s amongst patients with intestinal diseases associated with fat malabsorption, including post JI bypass. Early studies confirmed, as suspected, that the increased urinary oxalate came from dietary sources, since it could be prevented via use of a strict very low oxalate diet [36]. Amongst patients with ileal resection and fat malabsorption, the amount of urinary oxalate excretion correlated linearly with fecal fat content [37], and in individual patients fecal fat excretion, gastrointestinal absorption of labeled oxalate, and urinary oxalate excretion all fell when they were placed on a low fat diet [38]. Therefore, abnormal delivery of fat to the colon appears to be a key feature of this disorder that has been termed enteric hyperoxaluria.

Intracolonic calcium concentrations also appear to be a key determinant of oxalate absorption in the colon. In a small but intriguing study, calcium was infused directly into the colon of 3 patients with surgical resections, fat malabsorption and enteric hyperoxaluria [37]. Although the diets were not changed, and fecal fat remained constant, urinary oxalate levels fell, and then promptly reverted to baseline when the calcium infusions were stopped. One cannot usually infuse calcium directly into the colon, but oral administration of calcium supplements will increase calcium delivery to the colon since only a fraction will be absorbed. When JI bypass patients were placed on a higher calcium diet (3000 mg versus 800 mg), gastrointestinal absorption of oxalate fell and urinary oxalate levels similarly decreased [39]. Similar findings were documented on a 3000 mg versus 250 mg calcium diet [40]. In the latter study, even though urinary oxalate fell, urinary calcium levels also increased on the higher calcium diet. The net effect of these counter veiling changes on urinary supersaturation for calcium oxalate was not assessed, and therefore increased urinary calcium excretion while on high doses of oral calcium used as an oxalate binder remains a potential concern, and could potentially

neutralize any positive effect. In future studies, it will be important to carefully consider the net effect of oral calcium on urinary calcium oxalate supersaturation, in addition to urinary oxalate levels alone.

Based upon this older published data the standard treatment of this patient group has been a low fat, low oxalate diet with use of calcium supplements as an oxalate binder. If urinary citrate levels are reduced, use of oral potassium citrate also makes sense. Fortunately, data suggest that reversal of the JI-bypass, even many years out from the procedure, can often halt a decline in kidney function, and in many cases result in some modest longer-term improvement, as well as stop progression of the stone disease [41]. Therefore, it is still important to identify long term JI bypass patients with this complication as treatment options exist.

Hyperoxaluria and renal stones after RYGB

Little is known about the impact of most currently offered bariatric surgeries on the risk for nephrolithiasis. Since obesity and insulin resistance have been implicated as risk factors for nephrolithiasis, especially uric acid stones, one might reasonably hypothesize that RYGB could ameliorate kidney stone risk [8,29]. Further, the RYGB operation with a Roux limb < 150 cm in length has generally been believed not to cause fat malabsorption, thought to be a critical factor in the development of enteric hyperoxaluria.

However, we recently noted a seemingly large number of patients with calcium oxalate stones and relatively marked hyperoxaluria after RYGB in our institution. Therefore, in 2005 we conducted a systematic review of all Mayo Clinic patient records to identify potential cases of enteric hyperoxaluria in patients who had received RYGB between 1984–2005 (n=1436) [31]. In addition, a survey was sent to the subgroup that had undergone the potentially more malabsorptive distal RYGB (Roux limb ~300 cm and common channel length ~125 cm; n=258), since we hypothesized those patients might be more susceptible to this complication. A total of 23 cases of enteric hyperoxaluria were identified by the initial record review, 14 after proximal RYGB and 9 after distal RYGB. Most concerning were two patients that presented with renal failure and biopsy-proven oxalate nephropathy. Neither had a prior history of renal disease or nephrolithiasis. Amongst the distal RYGB group, 188/258 patients returned the supplemental survey. Of these 27 (16%) had experienced nephrolithiasis after the procedure; only 8 had had a stone preoperatively. We cannot reliably estimate the prevalence of stones in the proximal RYGB since they were not surveyed, many of these patients do not receive regular medical care at Mayo, and renal stones are not always recorded in the medical record. However, this study did suggest that nephrolithiasis was common after RYGB, and perhaps more so in the distal RYGB group.

In early 2006, we updated the Mayo Clinic series to include an increasing number of patients referred to our Stone Clinic after RYGB, and for whom we had detailed metabolic data [42]. A total of 60 patients were identified, including 31 who had been seen in the Stone Clinic. A large percentage (17/31) had been seen for the first time in stone clinic over the prior two years. The mean BMI of patients pre-operatively was 57 kg/m², with a decrease of 20 kg/m² at the time of the first stone event which averaged 2.9 years after RYGB. Although the distal RYGB only accounts for only ~18% of the total RYGB procedures performed at Mayo, there were 36 distal RYGB and 24 proximal RYGB patients identified. Therefore, patients may be at greater risk for stones after the distal procedure. Amongst those analyzed, stones were 100% calcium oxalate in 19 patients, and mixed uric acid/calcium oxalate in two other instances.

Amongst the subset seen in stone clinic, hyperoxaluria was commonly observed (present in 17/31), with a mean urine oxalate of 0.66 mM/24 hours (Table 1). Urinary citrate and calcium were modestly reduced, and overall urinary supersaturation for calcium oxalate was quite high. When divided into proximal and distal patients, there was no significant difference in urinary

parameters (Table 1). However, there did seem to be differences in the urine composition depending on time of presentation after RYGB. Those who presented less than 6 months postoperatively rarely had elevated urinary oxalate (mean 0.44 mM/day), whereas those longer than 6 months out often did (mean 0.77 mM/day; Figure 2). Urinary supersaturation was equally high in both groups however (Figure 2), due in large part to low urine volumes in the less than 6 month group. These differences may reflect changes in gastrointestinal function and diet that developed over the first year after the procedure.

In order to get a better sense regarding how common hyperoxaluria might be in the total group of patients that undergo RYGB, we next completed a small pilot study of patients randomly selected before (n=20), 6 months (n=8), and 12 months (n=13) after proximal RYGB. At baseline hyperoxaluria was rare (mean oxalate 0.35 mM/day) and urinary calcium oxalate supersaturation was not increased above the reference mean (Figure 3). Urinary composition was not significantly changed in the 6 months post operative group, but by 12 months mean urinary oxalate (0.74 mM/24 hrs) and calcium oxalate supersaturation were both elevated in this group of non-stone forming patients. Other urinary changes included a modest fall in urinary citrate and calcium (Table 1 and Figure 3). These data suggest that many patients may have sub clinical enteric hyperoxaluria and be at risk for stones after standard RYGB, since over half (7/13) were hyperoxaluric and nearly all (12/13) had elevated calcium oxalate supersaturation at the 12 months time point.

Other data is emerging that links RYGB to kidney stones. A very recent report lists urinary tract calculus as a common cause for emergency room visits (3.6%) and readmission to hospital (3.0%) within the first 180 days after bariatric surgery [43]. The University of Pittsburgh also recently examined their longer term experience with a specific focus on stone prevalence [44]. The medical records of a total of 972 persons that underwent RYGB between the years of 1997–2004 at their bariatric surgery center were examined for stone events, including review of radiology reports. In their group, 85 patients (8.8%) had a preoperative stone history. Of these, 26 (31.4%) had recurrent stones postoperatively (mean time 1.9 years), whereas an additional 31 developed stones *de novo* at a mean time of 2.8 years (3.5%). These data may underestimate the scope of the problem since stone history was obtained from record review alone and no information is provided regarding time or extent of follow-up in the cohort. Nevertheless, the data did suggest that stone prevalence was enriched by at least 70% in this population, compared to expected rates derived from Nutrition Examination Survey (NHANES) III data [44].

Recently, a large referral lab reported urinary chemistry values for 132 patients that were identified as having undergone “modern” bariatric surgery for obesity [45]. Only abbreviated patient history was available; for example the sub-type of surgery (e.g., banding versus gastric bypass) was not known. Nevertheless, the urinary data are remarkably similar to those observed in our patient group at Mayo Clinic. Mean urine oxalate was elevated (83 mg/day), with a corresponding increase in urinary calcium oxalate supersaturation (Table 1). Urine calcium excretion was slightly reduced, while citrate excretion and total volume were both fairly normal. Urine oxalate excretion was not as high as in an older group with *JI* bypass; nevertheless the calcium oxalate supersaturation was actually marginally higher in the modern bariatric group. Importantly, 23% of this referral lab cohort had a daily urinary oxalate excretion of greater than 100 mg, a level at which renal damage has been well described. Time to first stone was also comparable to the Mayo cohort (3.6 vs. 2.9 years) although relatively fewer had pre-existing stones (1/132 versus 11/31).

To our knowledge, no information is currently available to assess the relative potential risk for nephrolithiasis and/or hyperoxaluria after the various forms of bariatric surgery. However, very limited data are available regarding the degree of fat malabsorption in patients after selected

procedures [34]. After JI bypass overall fat absorption was reported to be only 15%, whereas it was 97% after VBG or LAGB. Fat absorption was also severely compromised after BPD, with or without duodenal switch (19%) and intermediate after RYGB (67%). Based upon this data, one might hypothesize that the risk for enteric hyperoxaluria would be greatest after BPD, lowest for VBG or LAGB, and intermediate for RYGB. However, even these inferences are tentative since the fat absorption numbers were based on measurements in only 9 patients in the RYGB group. We do note, however, that even though patients in the RYGB group had an elevated average of 44 grams of fecal fat (versus 139 grams in the BPD groups) the patients did not report prominent symptoms of diarrhea (average 1.5 bowel movements per day versus 3.6 in the BPD groups). This observation correlates with our personal clinical experience that the RYGB patients rarely report clinical diarrhea.

Treatment of nephrolithiasis after RYGB

Typical treatment strategies for enteric hyperoxaluria, as described above, are prescription of a low fat, low oxalate diet, generous fluid intake, use of oral oxalate binders such as calcium, and potassium citrate as a crystallization inhibitor. In practice these dietary modifications may be quite difficult to implement. For example, many patients have learned to alter their eating patterns after RYGB and consume many small meals and/or snacks in order to avoid dumping symptoms. Use of oxalate binders can be quite difficult under these circumstances. Although in general oxalate is found in green leafy vegetables, chocolate, nuts, strawberries, and soy products [46], accurate information regarding the oxalate content in particular foods is difficult to find since it is not measured routinely or listed on food labels. In addition, published values are general estimates, because oxalate content can vary depending on conditions during growth or manufacture. Therefore, avoiding high oxalate intake can require extensive education and patient motivation.

It is known that endogenous intestinal flora can metabolize oxalate [47]. For example, a subset of the population is colonized with *Oxalobacter formigenes* an obligate anaerobe that utilizes oxalate as its sole energy source. Several studies have suggested that colonization with *O. formigenes* is associated with lower urinary oxalate excretion, and that loss of colonization, for example due to antibiotic use, can increase urinary oxalate levels [48,49]. Whether or not RYGB procures alter colonization with this organism is unknown, however a single study demonstrated decreased intestinal colonization with these oxalate-degrading bacteria in patients after JI bypass [50]. Other intestinal bacteria could also alter oxalate fluxes, either via degradation within the lumen or effects on mucosal permeability and/or active absorption. A recent study demonstrated that oral administration of a mixed preparation of lactic acid bacteria with *in vitro* oxalate degrading capacity reduced urinary oxalate excretion by a small but significant percentage in a group of patients with enteric hyperoxaluria [51]. Oral administration of *O. formigenes* or its active oxalate-degrading enzymes represents another promising treatment strategy, because rats colonized with *O. formigenes* changed from net colonic absorbers of oxalate to net secretors [52]. A recent study supports the potential utility of such a strategy [53]. In a small group of patients with Primary Hyperoxaluria, a genetic disorder characterized by hepatic overproduction of oxalate, somewhat surprisingly an oral preparation of *O. formigenes* reduced both plasma oxalate concentrations and urinary oxalate excretions. Given the pathophysiology of the hyperoxaluria in these patients, one must speculate that increased colonic metabolism of oxalate resulted in increased net secretion of oxalate into the gastrointestinal tract, and hence its elimination from the body. These exciting results will require confirmation in larger and more diverse patient populations, but nevertheless provide intriguing insights into a novel treatment strategy.

Conclusions and future directions

As a first step, it will be vital to define the scope of the problem. How common is hyperoxaluria after RYGB or other forms of bariatric surgery? How many of these patients develop stones and/or renal damage? Based upon the preliminary data described above, it seems likely that the prevalence of hyperoxaluria and nephrolithiasis will be significant. Therefore, studies that can identify improved strategies to decrease urinary oxalate levels amongst the ever-expanding pool of patients undergoing RYGB surgery are clearly needed. Initially, it will be important to precisely determine the mechanism of hyperoxaluria in these patients. Is it strictly related to fat malabsorption? Are other factors involved, for example altered colonization with oxalate-degrading bacteria? Once these factors are identified, careful treatment trials with known or novel therapeutic agents are needed. Oral administration of oxalate-degrading bacteria, purified enzymes, or newly-developed oxalate-binding resins all seem feasible. In addition, since recent evidence suggests the intestinal anionic transporter *SLC26A6* is a key mediator of intestinal oxalate secretion [54], this membrane protein has emerged as an intriguing target for development of a drug that could enhance elimination of oxalate by the intestinal route.

If the incidence and severity of enteric hyperoxaluria described above is confirmed in prospective evaluations of larger numbers of post RYGB patients, preventative treatment strategies may be necessary in all patients following the surgery. In the meantime, as a minimum all patients who develop renal stones after RYGB should undergo prompt metabolic evaluation with initiation of appropriate treatments for stone prevention. Given the overall evidence that RYGB and other bariatric surgical procedures seem to benefit morbidly obese individuals [14,15], we do not currently consider the risk for hyperoxaluria and nephrolithiasis to be a contraindication for these surgeries. Rather, physicians caring for these patients need to be aware of this potential complication, factor it in when weighing the pros and cons of a surgical intervention in an individual patient, and have a low threshold to screen for it's development post operatively.

Acknowledgments

The authors acknowledge research support by grants from the National Institutes of Health (DK 73354, DK 77669, AR 30582, AT 002534, and DK 39337), and the Oxalosis and Hyperoxaluria Foundation.

Research Support: Grants from the National Institutes of Health (DK 73354, AR 30582, DK 77669, AT 002534, and DK 39337), the Oxalosis and Hyperoxaluria Foundation, and Mayo Foundation.

REFERENCES

1. Demaria EJ, Jamal MK. Surgical options for obesity. *Gastroenterol Clin North Am* 2005;34:127–142. [PubMed: 15823443]
2. Sarr MG, Felty CL, Hilmer DM, Urban DL, O'Connor G, Hall BA, Rooke TW, Jensen MD. Technical and practical considerations involved in operations on patients weighing more than 270 kg. *Arch Surg* 1995;130:102–105. [PubMed: 7802568]
3. Lopez-Jimenez F, Bhatia S, Collazo-Clavell ML, Sarr MG, Somers VK. Safety and efficacy of bariatric surgery in patients with coronary artery disease. *Mayo Clin Proc* 2005;80:1157–1162. [PubMed: 16178495]
4. Kim TH, Daud A, Ude AO, DiGiorgi M, Olivero-Rivera L, Schrope B, Davis D, Inabnet WB, Bessler M. Early U.S. outcomes of laparoscopic gastric bypass versus laparoscopic adjustable silicone gastric banding for morbid obesity. *Surg Endosc* 2006;20:202–209. [PubMed: 16341569]
5. Mehrotra C, Serdula M, Naimi TS, Khan LK, Miller J, Dietz W. Population-based study of trends, costs, and complications of weight loss surgeries from 1990 to 2002. *Obes Res* 2005;13:2029–2034. [PubMed: 16339136]
6. Sauerland S, Angrisani L, Belachew M, Chevallier JM, Favretti F, Finer N, Fingerhut A, Garcia Caballero M, Guisado Macias JA, Mittermair R, Morino M, Msika S, Rubino F, Tacchino R, Weiner

- R, Neugebauer EA. Obesity surgery: evidence-based guidelines of the European Association for Endoscopic Surgery (EAES). *Surg Endosc* 2005;19:200–221. [PubMed: 15580436]
7. Olbers T, Fagevik-Olsen M, Maleckas A, Lonroth H. Randomized clinical trial of laparoscopic Roux-en-Y gastric bypass versus laparoscopic vertical banded gastroplasty for obesity. *Br J Surg* 2005;92:557–562. [PubMed: 15810049]
8. Sjostrom L, Lindroos AK, Peltonen M, Torgerson J, Bouchard C, Carlsson B, Dahlgren S, Larsson B, Narbro K, Sjostrom CD, Sullivan M, Wedel H. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med* 2004;351:2683–2693. [PubMed: 15616203]
9. Patriti A, Facchiano E, Sanna A, Gulla N, Donini A. The enteroinsular axis and the recovery from type 2 diabetes after bariatric surgery. *Obes Surg* 2004;14:840–848. [PubMed: 15318993]
10. Stubbs RS, Wickremesekera SK. Insulin resistance in the severely obese and links with metabolic co-morbidities. *Obes Surg* 2002;12:343–348. [PubMed: 12082884]
11. Reinhold RB. Late results of gastric bypass surgery for morbid obesity. *J Am Coll Nutr* 1994;13:326–331. [PubMed: 7963136]
12. Klein S, Burke LE, Bray GA, Blair S, Allison DB, Pi-Sunyer X, Hong Y, Eckel RH. Clinical implications of obesity with specific focus on cardiovascular disease: a statement for professionals from the American Heart Association Council on Nutrition, Physical Activity, and Metabolism: endorsed by the American College of Cardiology Foundation. *Circulation* 2004;110:2952–2967. [PubMed: 15509809]
13. Gleysteen JJ. Results of surgery: long-term effects on hyperlipidemia. *Am J Clin Nutr* 1992;55:591S–593S. [PubMed: 1733134]
14. Sjostrom L, Narbro K, Sjostrom CD, Karason K, Larsson B, Wedel H, Lystig T, Sullivan M, Bouchard C, Carlsson B, Bengtsson C, Dahlgren S, Gummesson A, Jacobson P, Karlsson J, Lindroos AK, Lonroth H, Naslund I, Olbers T, Stenlof K, Torgerson J, Agren G, Carlsson LM. Effects of bariatric surgery on mortality in Swedish obese subjects. *N Engl J Med* 2007;357:741–752. [PubMed: 17715408]
15. Adams TD, Gress RE, Smith SC, Halverson RC, Simper SC, Rosamond WD, Lamonte MJ, Stroup AM, Hunt SC. Long-term mortality after gastric bypass surgery. *N Engl J Med* 2007;357:753–761. [PubMed: 17715409]
16. Gastrointestinal surgery for severe obesity. Consensus Development Conference Panel. *Ann.Int.Med* 1991;115:956–961. [PubMed: 1952493]
17. Sarr MG, Balsiger BM. Bariatric surgery in the 1990's. *Swiss Surg* 2001;7:11–15. [PubMed: 11234310]
18. Kendrick ML, Dakin GF. Surgical approaches to obesity. *Mayo Clin Proc* 2006;81:S18–24. [PubMed: 17036575]
19. Howard L, Malone M, Michalek A, Carter J, Alger S, Van Woert J. Gastric Bypass and Vertical Banded Gastroplasty- a Prospective Randomized Comparison and 5-Year Follow-up. *Obes Surg* 1995;5:55–60. [PubMed: 10733794]
20. Chapman AE, Kiroff G, Game P, Foster B, O'Brien P, Ham J, Maddern GJ. Laparoscopic adjustable gastric banding in the treatment of obesity: a systematic literature review. *Surgery* 2004;135:326–351. [PubMed: 14976485]
21. Bouldin MJ, Ross LA, Sumrall CD, Loustalot FV, Low AK, Land KK. The effect of obesity surgery on obesity comorbidity. *Am J Med Sci* 2006;331:183–193. [PubMed: 16617233]
22. Benotti PN, Wood GC, Rodriguez H, Carnevale N, Liriano E. Perioperative outcomes and risk factors in gastric surgery for morbid obesity: a 9-year experience. *Surgery* 2006;139:340–346. [PubMed: 16546498]
23. Livingston EH. Complications of bariatric surgery. *Surg Clin North Am* 2005;85:853–868. vii. [PubMed: 16061090]
24. Balsiger BM, Kennedy FP, Abu-Lebdeh HS, Collazo-Clavell M, Jensen MD, O'Brien T, DHensrud DD, Dinneen SF, Thompson GB, Que FG, Williamns DE, Clark MW, Grnat JE, Frick MS, Mueller RA, Maj JL, Sarr MG. Prospective Evaluation of Roux-en-Y Gastric Bypass as Primary Operation for Medically Complicated Obesity. *Mayo Clin Proc* 2000;75:673–680. [PubMed: 10907381]
25. Mason ME, Jalagani H, Vinik AI. Metabolic complications of bariatric surgery: diagnosis and management issues. *Gastroenterol Clin North Am* 2005;34:25–33. [PubMed: 15823436]

26. De Prisco C, Levine SN. Metabolic bone disease after gastric bypass surgery for obesity. *Am J Med Sci* 2005;329:57–61. [PubMed: 15711420]
27. Collazo-Clavell ML, Jimenez A, Hodgson SF, Sarr MG. Osteomalacia after Roux-en-Y gastric bypass. *Endocr.Pract* 2004;10:195–198. [PubMed: 15310536]
28. Chaves LC, Faintuch J, Kahwage S, Alencar Fde A. A cluster of polyneuropathy and Wernicke-Korsakoff syndrome in a bariatric unit. *Obes Surg* 2002;12:328–334. [PubMed: 12082882]
29. Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, Schoelles K. Bariatric surgery: a systematic review and meta-analysis. *Jama* 2004;292:1724–1737. [PubMed: 15479938]
30. Flum DR, Salem L, Elrod JA, Dellinger EP, Cheadle A, Chan L. Early mortality among Medicare beneficiaries undergoing bariatric surgical procedures. *Jama* 2005;294:1903–1908. [PubMed: 16234496]
31. Nelson WK, Houghton SG, Milliner DS, Lieske JC, Sarr MG. Enteric hyperoxaluria, nephrolithiasis, and oxalate nephropathy: potentially serious and unappreciated complications of Roux-en-Y gastric bypass. *Surgery for Obesity and Related Diseases* 2005;1:481–485. [PubMed: 16925274]
32. Griffen WO Jr. Bivins BA, Bell RM. The decline and fall of the jejunioleal bypass. *Surg Gynecol Obstet* 1983;157:301–308. [PubMed: 6623319]
33. Requarth JA, Burchard KW, Colacchio TA, Stukel TA, Mott LA, Greenberg ER, Weismann RE. Long-term morbidity following jejunioleal bypass. The continuing potential need for surgical reversal. *Arch Surg* 1995;130:318–325. [PubMed: 7887801]
34. Puzziferri N, Blankenship J, Wolfe BM. Surgical treatment of obesity. *Endocrine* 2006;29:11–19. [PubMed: 16622288]
35. Parks JH, Worcester EM, O'Connor RC, Coe FL. Urine stone risk factors in nephrolithiasis patients with and without bowel disease. *Kidney Int* 2003;63:255–265. [PubMed: 12472791]
36. Earnest DL, Johnson G, Williams HE, Admirand WH. Hyperoxaluria in patients with ileal resection: an abnormality in dietary oxalate absorption. *Gastroenterology* 1974;66:1114–1122. [PubMed: 4829118]
37. Modigliani R, Labayle D, Aymes C, Denvil R. Evidence for excessive absorption of oxalate by the colon in enteric hyperoxaluria. *Scand J Gastroent* 1978;13:187–192. [PubMed: 635458]
38. Andersson H, Bosaeus I. Hyperoxaluria in malabsorptive states. *Urol Int* 1981;36:1–9. [PubMed: 7020204]
39. Hylander E, Jarnum S, Nielsen K. Calcium treatment of enteric hyperoxaluria after jejunioleal bypass for morbid obesity. *Scand J Gastroent* 1980;15:349–352. [PubMed: 7433895]
40. Stauffer JQ. Hyperoxaluria and intestinal disease. The role of steatorrhea and dietary calcium in regulating intestinal oxalate absorption. *Am J Dig Dis* 1977;22:921–928. [PubMed: 920694]
41. Dhar NB, Grundfest S, Jones JS, Streem SB. Jejunioleal bypass reversal: effect on renal function, metabolic parameters and stone formation. *J Urol* 2005;174:1844–1846. discussion 1846. [PubMed: 16217311]
42. Sinha MK, Collazo-Clavell ML, Rule A, Milliner DS, Nelson W, Sarr MG, Kumar R, Lieske JC. Hyperoxaluric nephrolithiasis is a complication of Roux-en-Y gastric bypass surgery. *Kidney Int* 2007;72:100–107. [PubMed: 17377509]
43. Encinosa WE, Bernard DM, Chen CC, Steiner CA. Healthcare utilization and outcomes after bariatric surgery. *Med Care* 2006;44:706–712. [PubMed: 16862031]
44. Durrani O, Morrisroe S, Jackman S, Averch T. Analysis of stone disease in morbidly obese patients undergoing gastric bypass surgery. *J Endourol* 2006;20:749–752. [PubMed: 17094749]
45. Asplin JR, Coe FL. Hyperoxaluria in kidney stone formers treated with modern bariatric surgery. *J Urol* 2007;177:565–569. [PubMed: 17222634]
46. Parmar MS. Kidney stones. *Bmj* 2004;328:1420–1424. [PubMed: 15191979]
47. Argenzio RA, Liacos JA, Allison MJ. Intestinal oxalate-degrading bacteria reduce oxalate absorption and toxicity in guinea pigs. *J Nutr* 1988;118:787–792. [PubMed: 3373343]
48. Siener R, Ebert D, Hesse A. Urinary oxalate excretion in female calcium oxalate stone formers with and without a history of recurrent urinary tract infections. *Urol Res* 2001;29:245–248. [PubMed: 11585279]

49. Sidhu H, Schmidt ME, Cornelius JG, Thamilselvan S, Khan SR, Hesse A, Peck AB. Direct correlation between hyperoxaluria/oxalate stone disease and the absence of the gastrointestinal tract-dwelling bacterium *Oxalobacter formigenes*: possible prevention by gut recolonization or enzyme replacement therapy. *J.Am.Soc.Nephrol* 1999;10:S334–S340. [PubMed: 10541258]
50. Allison MJ, Cook HM, Milne DB, Gallagher S, Clayman RV. Oxalate degradation by gastrointestinal bacteria from humans. *J Nutr* 1986;116:455–460. [PubMed: 3950772]
51. Lieske JC, Goldfarb DS, De Simone C, Regnier C. Use of a probiotic to decrease enteric hyperoxaluria. *Kidney Int* 2005;68:1244–1249. [PubMed: 16105057]
52. Hatch M, Cornelius J, Allison M, Sidhu H, Peck A, Freel RW. *Oxalobacter* sp. reduces urinary oxalate excretion by promoting enteric oxalate secretion. *Kidney Int* 2006;69:691–698. [PubMed: 16518326]
53. Hoppe B, Beck B, Gatter N, von Unruh G, Tischer A, Hesse A, Laube N, Kaul P, Sidhu H. *Oxalobacter formigenes*: a potential tool for the treatment of primary hyperoxaluria type 1. *Kidney Int* 2006;70:1305–1311. [PubMed: 16850020]
54. Freel RW, Hatch M, Green M, Soleimani M. Ileal oxalate absorption and urinary oxalate excretion are enhanced in *Slc26a6* null mice. *Am J Physiol Gastrointest Liver Physiol* 2006;290:G719–728. [PubMed: 16373425]

Figure 1. Commonly-used weight loss procedures

Panel A: Laparoscopic adjustable gastric band (LAGB). **Panel B:** Vertical banded gastroplasty (VBG). **Panel C:** Proximal Roux-en Y gastric bypass (RYGB). **Panel D:** Distal RYGB. **Panel E:** Biliopancreatic diversion with the duodenal switch (BPD-DS). See text for discussion.

Figure 2. Urine oxalate excretion and calcium oxalate supersaturation amongst those stone formers who present early (<6 months) or late (> 6 months) after RYGB

Hyperoxaluria was more prominent amongst those that presented later (**Panel A**), although calcium oxalate supersaturation was equally high in the <6 months group largely due to lower urine volumes (**Panel B**). Adapted from [42].

Figure 3. Urine chemistries amongst a random sampling of patients before (n=20), 6 months after (n=8) and 12 months after (n=13) RYGB

Hyperoxaluria was common at 12 but not 6 months (**Panel A**) with a corresponding increase in urinary calcium oxalate supersaturation (**Panel D**). Urine volume (**Panel B**), citrate and calcium excretions (**Panel C**) also fell postoperatively. These data suggest that many patients may be at risk for calcium oxalate stones after this procedure. Adapted from [42].

Urinary Chemistries in patients with and without gastric bypass surgery

Table 1

	Asplin and Coe [45]				Sinha et al [42]						
	Normal		Stone formers		"Modern Bariatric"		RYGB with stones	RYGB: cross section			
	Male n=96	Female n=72	Male n=1330	Female n=718	Male n=17	Female n=10	Male n=28	Female n=104	Pre-op n=20	6 mos n=8	12 mos n=13
Oxalate (mg/day)	37	28	42	33	109	96	92	73	34	31	73
Calcium (mg/day)	187	150	237	192	135	95	140	143	206	111	112
Citrate (mg/day)	497	607	529	506	202	341	524	396	660	563	444
pH	6.06	6.03	5.99	6.05	5.63	5.54	5.71	5.75	5.95	5.81	5.76
Volume (L/day)	1.52	1.41	1.74	1.50	1.97	1.73	1.75	1.52	1.93	1.41	1.63
SS CaOx	8.1	6.6	9.1	8.9	8.8	9.0	10.6	13.6	4.0	4.3	6.9