

Hyperoxaluria and Bariatric Surgery

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Abstract. Bariatric surgery as a means to treat obesity is becoming increasingly common in the United States. An early form of bariatric surgery, the jejunoileal bypass, had to be abandoned in 1980 due to numerous complications, including hyperoxaluria and kidney stones. Current bariatric procedures have not been systematically evaluated to determine if they cause hyperoxaluria. Presented here are data showing that hyperoxaluria is the major metabolic abnormality in patients with bariatric surgery who form kidney stones. Further studies are needed to assess the prevalence of hyperoxaluria in all patients with bariatric surgery.

Keywords: Nephrolithiasis, Obesity, Kidney Failure, Oxalate

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INTRODUCTION

Extreme obesity is associated with multiple medical problems and it has been demonstrated that mortality increases significantly when body mass index (defined as height in cm/weight in kg) is above 35 [1]. Medical co-morbidities such as diabetes mellitus, hyperlipidemia, sleep apnea, hypertension and arthritis reduce the quality of life as well as shortening life span. Although many dietary and lifestyle programs have shown success inducing weight loss acutely, there is little data to support that such programs maintain long term weight loss and the expected health benefits for those who use the programs. Bariatric surgery developed in response to the lack of success of diet and lifestyle changes in effectively reducing weight.

The first common bariatric procedure was the jejunoileal (JI) bypass [2]. In this surgery, the proximal 35 cm of the jejunum is anastomosed to the ileum 10 cm from the ileocecal valve, providing very little intestinal surface area for absorption. The altered intestinal physiology did result in significant weight loss, but the accompanying malabsorption of vitamins, bile acids, fats, and other nutrients led to a number of complications. Many subjects suffered from liver disease, arthritis, vitamin deficiencies, bone disease, and kidney stones [3]. Hyperoxaluria was determined to be the etiology of the kidney stones. The malabsorbed fatty acids would bind intestinal oxalate, leaving a greater portion of intestinal oxalate free to be absorbed. In addition, reduced absorption of bile salts in the small intestine delivered abnormal amounts of bile salts to the colon, which damaged the colonic mucosa making it more permeable to oxalate. The combined effect of these two factors led to an increase in absorption of dietary oxalate [4]. Kidney stones were quite common, and hyperoxaluria could be so severe to lead to kidney damage, and in the most extreme cases, kidney failure. Due to

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the significant level of complications, the FDA banned the jejunoileal bypass in 1980. However, 25,000 JI bypasses had been performed prior to the ban and patients continued to present with complications for years after. Many of the bypasses needed to be surgically revised to relieve the side effects [3].

When JI bypass was banned a new bariatric procedure was needed for patients with severe obesity. The Roux-en-y gastric bypass, which had first been introduced as a treatment for obesity by Mason and Ito in 1967, became the new bariatric procedure of choice [5]. Gastric bypass induces weight loss by restricting the size of the gastric reservoir, altering caloric intake by inducing dumping syndrome in response to high carbohydrate meals, and by causing a feeling of anorexia. Later, other bariatric procedures were introduced, some focused on restricting caloric intake by reducing the size of the stomach, such as gastric banding, and other procedures caused some degree of malabsorption, such as the very long limb gastric bypass and the biliopancreatic diversion. However, none of the procedures were felt to lead to the severe degree of malabsorption seen with JI bypass and therefore complication rates were less, and the risk of hyperoxaluria and stone disease were considered small.

Prevalence of obesity has increased dramatically over the last 20 years. Based on data from the NHANES studies, approximately 15% of the population had BMIs in the obese range from 1962 to 1985 [6]. However, in the NHANES study of 1994 and the most recent data from 2000 there was a clear increase in the rate of obesity, reaching 30% of the adult population by the 2000 survey. From 1994 to 2000 there was a 40% increase in the rate of extreme obesity (defined as a BMI >40). As would be expected, as the rate of obesity in the US increased, so has the rate of bariatric surgery. From 1998 to 2002, bariatric surgery increased 3 fold from approximately 20,000 procedures to over 60,000 procedures [7]. Over that time period the most common procedure performed was a gastric bypass, accounting for approximately 80% of bariatric surgery cases. Biliopancreatic diversion and pure restrictive procedures accounted for the rest, being performed at about equal rates.

MODERN BARIATRIC SURGERY AND HYPEROXALURIA

Despite the great increase in bariatric surgery, only one study attempted to measure urine oxalate excretion in patients with bariatric surgery other than JI bypass. In 1981, Hofmann et al reported urine oxalate excretion rates in 22 patients who had undergone biliopancreatic diversions, compared with a set of control patients, all spouses of the patients [8]. Only one surgical met their definition of hyperoxaluria. However, sparse data are provided about the study design, such as gender of the subjects, time from bariatric surgery and any dietary data, nor was any statistical analysis provided as to whether the bariatric surgery patients' urine oxalate excretion was different than the controls. Overall, there is little known about the risk of stone disease after bariatric surgery.

A study from the Mayo clinic was one of the first to suggest a link between bariatric surgery and kidney stones [9]. In 2005 Nelson et al reported on 23 patients who they classified as having enteric hyperoxaluria diagnosed after having bariatric surgery. The

series included both patients with the standard Roux-en-Y gastric bypass as well as patients with the very long limb gastric bypass, a procedure felt to result in some degree of malabsorption and more significant weight loss. Twenty one of the twenty three patients presented with kidney stones and the vast majority were found to have hyperoxaluria when urine chemistries were measured. Of those presenting with kidney stones, the mean urine oxalate excretion rate was 85 mg/day. Two of the patients presented with acute kidney failure and were found to have oxalosis on kidney biopsy. This study is a retrospective review of those subjects who presented with renal problems after bariatric surgery. In order to estimate the prevalence of such renal problems in the bariatric surgery population the investigators performed a survey of all subjects who had the very long limb gastric bypass at the Mayo Clinic. Of the 258 subjects they attempted to contact, 73% responded, of which 16% developed kidney stones after the bariatric surgery. This work supports the premise that hyperoxaluria and kidney stones are a complication of gastric bypass surgery and that some of these patients are at risk for kidney damage from severe hyperoxaluria.

We have also undertaken a study to determine if hyperoxaluria may be a complication of modern bariatric procedures [10]. Using a database from a clinical laboratory specializing in measuring urine chemistries in kidney stone patients (Litholink Corporation, Chicago IL), we identified all patients who had reported prior bariatric surgery. 132 patients were identified as having bariatric surgery after 1980. We did not attempt to classify the type of surgery as we were not confident that patients could reliably distinguish the types of surgery. We compared the urine chemistries to normal subjects, routine stone forming patients without a history of bowel disease or intestinal surgery, and patients who had JI bypass surgery. Patients with modern bariatric surgery had urine oxalate excretion nearly double that of non-stone forming subjects and routine stone forming patients (Figure 1), though not quite as high as had been seen with JI bypass procedures. Calcium oxalate supersaturation, the driving force for crystallization, was even higher in patients with modern bariatric surgery than JI bypass, as the modern bariatric patients had slightly higher urine calcium and lower urine volumes.

Since our study only contains post-surgery urine chemistries, it could be possible that hyperoxaluria is a characteristic of patients with severe obesity and that we are incorrect in assigning the cause of the hyperoxaluria to the weight loss surgery. Lemann et al showed that urine oxalate excretion increases with body weight, though none of the subjects in his study had the level of hyperoxaluria we report, nor were they chosen for obesity [11]. Taylor et al have reported that risk of kidney stone disease increases with BMI, though urine chemistry data was not available to determine if hyperoxaluria played a role in this phenomenon [12]. To address this issue, we compared female patients with bariatric surgery (n = 104) to routine female stone formers from the Litholink data base, chosen over a two month period, who weighed more than 100 kg (n = 56). The bariatric surgery group weighed 94 kg on average at the time of the evaluation and had a urine oxalate excretion of 73 mg/d, whereas the obese stone forming patients had an average weight of 120 kg but had a

mean oxalate excretion of only 36 mg/d (Figure 2). It seems unlikely that obesity by itself explains the hyperoxaluria seen in the bariatric surgery patients.

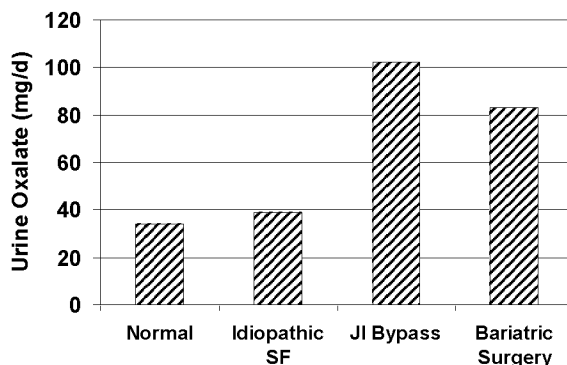


FIGURE 1. Comparison of urine oxalate excretion in normal subjects, idiopathic stone forming patients, patients with jejunioleal bypass and patients with modern bariatric surgery.

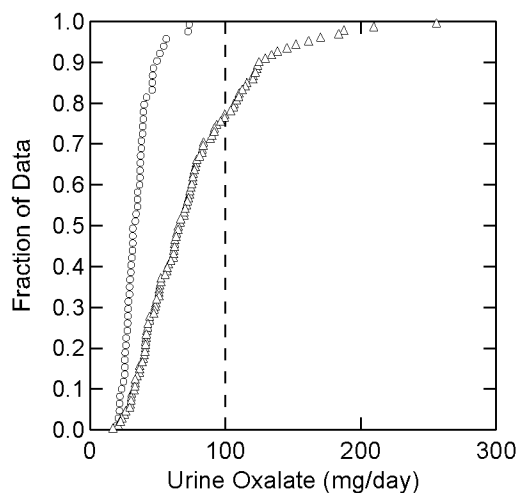


FIGURE 2. Quantile plot of urine oxalate excretion in women with bariatric surgery (triangles) and women with idiopathic kidney stone disease (open circles). Women with bariatric surgery have much higher urine oxalate, with over 20% having a urine oxalate greater than 100 mg/day.

Another way to address the effect of bariatric surgery on urine oxalate excretion would be to determine urine oxalate excretion before and after bariatric surgery. There have been no reports in the literature of oxalate measured pre and post bariatric surgery. Figure 3 shows data from two such patients identified from my own clinical

experience. Both patients had a history of kidney stones and had urine chemistries measured as part of routine medical care. Both patients had Roux-en-Y gastric bypass. As can be seen in the figure, both patients had significant and persistent elevations of urine oxalate after their surgery. Stone formation rates also increased after the bariatric surgery.

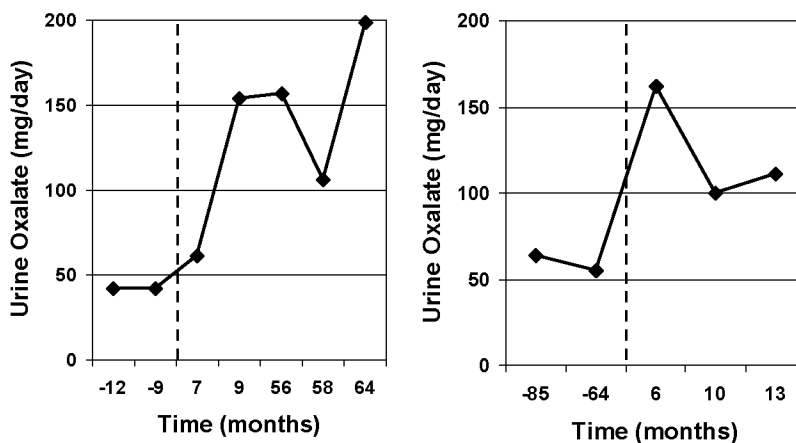


FIGURE 3. Urine oxalate excretion in two patients who had urine oxalate measured prior to gastric bypass surgery and subsequent to the surgery. The vertical dashed line shows the time of the gastric bypass surgery.

DISCUSSION

There are limitations to the data presented here. The studies are retrospective and are subject to bias. The patients included in the studies all presented with either kidney stones or kidney failure, there is not a random sampling of bariatric surgery patients to determine the frequency of hyperoxaluria. Thus, the patients presented may be representative of only a small portion of the total population of bariatric surgery patients. In addition, our data did not allow us to analyze patients based on the type of surgery performed. It seems likely that the different surgical procedures will carry varying degrees of risk for hyperoxaluria. Cross-sectional studies comparing oxalate excretion in patients with various bariatric procedures, as well as prospective studies measuring urine oxalate before and after bariatric surgery are needed to fully delineate the extent of the problem. The data we presented here does supply evidence that there are some patients who develop hyperoxaluria and kidney stones as a result of bariatric surgery. A recent study by Encinosa et al found nephrolithiasis to be the 9th most common cause of emergency room visit in the 6 months post bariatric surgery [13]. Since the rate of bariatric surgery continues to increase, stone rates are likely to increase and more research will be needed to define the extent of this problem.

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