BRIEF REPORT

The risk of kidney stones following bariatric surgery: a systematic review and meta-analysis

Charat Thongprayoona, Wisit Cheungpasitpornb, Priya Vijayvargiay, Pimjai Anthanontc,d and Stephen B. Ericksona

aDivision of Nephrology and Hypertension, Mayo Clinic, Rochester, MN, USA; bDepartment of Internal Medicine, Mayo Clinic, Rochester, MN, USA; cDivision of Endocrinology, Mayo Clinic, Rochester, MN, USA; dFaculty of Medicine, Thammasat University Hospital, Bangkok, Thailand

ABSTRACT

Background With rising prevalence of morbid obesity, the number of bariatric surgeries performed each year has been increasing worldwide. The objective of this meta-analysis was to assess the risk of kidney stones following bariatric surgery. Methods A literature search was performed using MEDLINE, EMBASE, and Cochrane Database of Systematic Reviews from inception through July 2015. Only studies reporting relative risks, odd ratios or hazard ratios (HRs) to compare risk of kidney stones in patients who underwent bariatric surgery versus no surgery were included. Pooled risk ratios (RR) and 95% confidence interval (CI) were calculated using a random-effect, generic inverse variance method. Results Four studies (One randomized controlled trial and three cohort studies) with 11,348 patients were included in analysis to assess the risk of kidney stones following bariatric surgery. The pooled RR of kidney stones in patients undergoing bariatric surgery was 1.22 (95% CI, 0.63–2.35). The type of bariatric surgery subgroup analysis demonstrated an increased risk of kidney stones in patients following Roux-en-Y gastric bypass (RYGB) with the pooled RR of 1.73 (95% CI, 1.30–2.30) and a decreased risk of kidney stones in patients following restrictive procedures including laparoscopic banding or sleeve gastrectomy with the pooled RR of 0.37 (95% CI, 0.16–0.85). Conclusions Our meta-analysis demonstrates an association between RYGB and increased risk of kidney stones. Restrictive bariatric surgery, on the other hand, may decrease kidney stone risk. Future study with long-term follow-up data is needed to confirm this potential benefit of restrictive bariatric surgery.

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Introduction

Kidney stones are one of the most common urological problems. The incidence of kidney stones is increasing with an estimated prevalence of 10% to 15% worldwide.1–4 In the United States, approximately 13% of men and 7% of women will develop a kidney stone during their life time,5 and more than $2 billion are spent annually on treatment.6

Obesity has increasingly become a major public health problem worldwide. In 2012, more than one-third (34.9% or 78.6 million) of U.S. adults are obese.7 Bariatric surgery is associated with improved long-term survival in morbidly obese patients.8 Not surprising, the number of bariatric procedures performed annually has increased globally to 468,609 procedures in 2013,9 with Roux-en-Y gastric bypass (RYGB) as the most common procedure, followed by sleeve gastrectomy, laparoscopic adjustable gastric banding, and biliopancreatic diversion with duodenal switch. Despite lack of controls, studies have identified kidney stones as a well-known complication of purely malabsorptive bariatric procedures, such as Jejunoileal bypass.10–12 However, the findings of studies evaluating the risk of kidney stones in patients following modern bariatric surgery are conflicting.13 Several studies have demonstrated an increased risk of kidney stones in patients following bariatric surgery.14,15 Conversely, not with standing a relative-short follow-up time, several studies have shown no associations16 or lower risk of kidney stones in patients following bariatric surgery.17 The objective of this meta-analysis was to evaluate the risk of kidney stones in patients who underwent bariatric surgery.

Methods

Search strategy

Two investigators (C.T. and W.C.) independently searched published studies indexed in MEDLINE,
EMBASE and the Cochrane database from inception through July 2015 using the search strategy described in Item S1 in online supplementary data. A manual search for additional relevant studies using references from retrieved articles was also performed. In order to assess the quality and publication bias of all studies, conference abstracts and unpublished studies were excluded.

Inclusion criteria

The inclusion criteria were as follows: (1) RCTs or observational studies (case-control, cross-sectional or cohort studies) published as original studies to evaluate the risk of kidney stones in patients following bariatric surgery, (2) studies that provided data to calculate odds ratios, relative risks, hazard ratios or standardized incidence ratio with 95% confidence intervals (CI) were provided, and (3) a reference group composed of participants who did not have bariatric surgery. No limits were applied for language.

Study eligibility was independently determined by the two investigators noted above. Differing decisions were resolved by mutual consensus. The quality of each study was independently evaluated by each investigator using Jadad quality assessment scale \(^{18}\) for RCTs and Newcastle-Ottawa quality assessment scale \(^{19}\) for observational studies.

Data extraction

The two investigators utilized a standardized data collection form to extract the following information: last name of the first author, study design, year of study, country of origin, year of publication, sample size, characteristics of included participants, definition of bariatric surgery, type of bariatric surgery, method used to diagnose kidney stones, confounder adjustment and adjusted effect estimates with 95% CI.

Statistical analysis

Review Manager 5.3 software from the Cochrane Collaboration (Copenhagen, Denmark) was used for data analysis. Point estimates and standard errors were extracted from individual studies and were combined by the generic inverse variance method of DerSimonian and Laird. \(^{20}\) Given the high likelihood of inter study variances, we used a random-effect model rather than a fixed-effect model. Statistical heterogeneity was assessed using the Cochran’s Q test. This statistic is complemented with the \(I^2\) statistic, which quantifies the proportion of the total variation across studies that is due to heterogeneity rather than chance. A value of \(I^2\) of 0% to 25% represents insignificant heterogeneity, 26% to 50% low heterogeneity, 51% to 75% moderate heterogeneity, and >75% high heterogeneity. \(^{21}\) The presence of publication bias was assessed by funnel plots of the logarithm of odds ratios versus their standard errors. \(^{22}\)

Results

Our search strategy yielded 391 potentially relevant articles. Four studies (one RCT \(^{16}\) and three cohort studies \(^{14,15,17}\) with 11,348 patients were included in analysis to assess the risk of kidney stones following bariatric surgery. Of four studies, three studied the risk of kidney stones in patients following RYGB. \(^{14-16}\) The risk of kidney stones following restrictive procedures including laparoscopic banding and sleeve gastrectomy were assessed in two studies. \(^{15,17}\) An observational study reported a risk of kidney stones following malabsorptive procedures including very-long limb RYGB or biliopancreatic diversion with duodenal switch. \(^{15}\) Figure 1 outlines our search methodology and selection process. Table 1 describes the detailed characteristics and quality assessment of the included studies.

The risk of kidney stones in patients following bariatric surgery

The pooled RR of kidney stones in patients following bariatric surgery was 1.22 (95% CI, 0.63–2.35, \(I^2 = 83\%\)). Figure 2 shows the forest plot of the included studies. However, when prespecified subgroup analysis of bariatric surgery type was performed, the risk of kidney stones in patients following RYGB was pooled RR of 1.73 (95% CI, 1.30–2.30) as shown in Figure 3. The statistical heterogeneity was low with an \(I^2\) of 26%. Approximate follow-up time was 3–6 years as demonstrated in Table 1. The risk of kidney stones was significantly decreased in patients following restrictive procedures with the pooled RR of 0.37 (95% CI, 0.16–0.85), compared to the patients who did not have surgery (Figure 4) with approximate follow-up time of 2 to 4 years. The statistical heterogeneity was insignificant with an \(I^2\) of 0%. The data on the risk of kidney stones following malabsorptive procedures including very-long limb RYGB or biliopancreatic diversion with duodenal switch were limited; 1 observational study reported an increased risk of kidney stones with HR of 4.15 (2.16–8.00).

Evaluation for publication bias

Funnel plots to evaluate publication bias for the risk of kidney stones in patients following bariatric surgery, RYGB and restrictive procedures are summarized in
Discussion

The findings in our meta-analysis demonstrate that the risk of kidney stones following bariatric surgery is different depending on the type of surgery. The prespecified subgroup analysis showed an overall 1.73-fold increased risk of kidney stones in patients following RYGB compared to those who did not have surgery. Interestingly, we found a 0.37-fold decreased kidney stone risk in patients following restrictive procedures including laparoscopic banding or sleeve gastrectomy.

Epidemiologic studies have demonstrated an association between obesity and kidney stones. Obesity is associated with increased urinary calcium and oxalate excretions leading to calcium oxalate crystallization. In addition, obesity-related insulin resistance can limit renal ammoniagenesis and subsequently cause acidic urine, resulting in higher risk of uric acid stone formation. Bariatric surgery has been shown to be an effective treatment for weight loss. However, different types of bariatric surgery carry individual risk of developing kidney stones as revealed in our meta-analysis. Although RYGB is considered as a mixed restrictive and malabsorptive procedure, standard RYGB (Roux-en-Y limb = 150 cm) causes less malabsorption compared to very-long limb RYGB. However, studies have still found significant hyperoxaluria in patients following...
| Country     | Matlaga et al.\textsuperscript{14} | Semins et al.\textsuperscript{17} | Schauer et al.\textsuperscript{16} | Lieske et al.\textsuperscript{15} |
|-------------|----------------------------------|----------------------------------|-----------------------------------|----------------------------------|
| Study design| USA Cohort study                 | USA Cohort study                 | USA RCT                           | USA Cohort study                 |
| Year        | 2009                             | 2009                             | 2014                              | 2015                             |
| Total number| 9278                             | 402                              | 150                               | 1518                             |
| Procedure group | Patients undergoing Roux-en-Y gastric bypass surgery for bariatric surgery; median F/U = 4.6 (0.008) years | Patient undergoing gastric banding: median F/U = 2.3 (0.06) years | Obese patients (BMI 27-43 kg/m\textsuperscript{2}) with uncontrolled type 2 DM receiving: 
  - Intensive medical therapy plus Roux-en-Y gastric bypass 
  - Intensive medical therapy plus sleeve gastrectomy 
  Outcome assessment at 3 years. | Patients undergoing bariatric surgery: 
  - Roux-en-Y gastric bypass (78%); mean F/U = 6.2 (3.1) years 
  - Malabsorptive procedures including very long limb RYGB or bilipancreatic diversion/duodenal switch (14%); mean F/U = 6.2 (3.7) 
  - Restrictive procedures including laparoscopic banding or sleeve gastrectomy (7%); mean F/U = 3.9 (1.6) |
| Control group | Matched obese patients with BMI > 35 kg/m\textsuperscript{2} who did not have surgery | Matched obese patients with BMI > 35 kg/m\textsuperscript{2} who did not have surgery | Obese patients with uncontrolled type 2 DM receiving intensive medical therapy alone | Matched obese subject with BMI > 35 kg/m\textsuperscript{2} who did not have surgery |
| Renal/urinary stone ascertainment | DRG code (323, 324) and ICD-9 code (274.11, 592, 592.0, 592.1, 592.9) | DRG code (323, 324) and ICD-9 code (274.11, 592, 592.0, 592.1, 592.9) | OR for all bariatric surgery 0.62 (0.20–1.86) 
OR for Roux-en-Y gastric bypass 0.69 (0.19–2.43) 
OR for sleeve gastrectomy 0.55 (0.14–2.09) | ICD-9 code (592, 594, 274.11) |
| Adjusted OR or RR | 1.71 (1.44–2.04) | 0.24 (0.07–0.86) | HR for all bariatric surgery 2.73 (1.79–4.17) 
HR for RYGB 2.13 (1.30–3.49) | HR for malabsorptive procedures 4.15 (2.16–8.00) 
HR for restrictive procedures 0.46 (0.06–3.45) |
| Confounder adjusted | Matching for age, sex, diagnosis of DM and HTN prior to index surgery date | Matching for age, sex, diagnosis of DM and HTN prior to index surgery date | Randomization | Matching for sex, BMI and index year 
Adjusted for age, sex and other baseline comorbidities (hypertension, DM, arthritis, and sleep apnea) |
| Quality assessment | Selection:4, Comparability:2, Outcome:3 | Selection:4, Comparability:2, Outcome:3 | Randomization: 2, Blinding: 0, Follow-up: 1 | Selection:4, Comparability:2, Outcome:3 |

Abbreviation: BMI, body mass index; DM, diabetes mellitus; GFR, glomerular filtration rate; LVEF, left ventricular ejection fraction; NR, not report; DRG, Diagnosis Related Group; RCT, randomized controlled trial.
standard RYGB, particularly six months after the procedure. Although the underlying explanation(s) of hyperoxaluria in RYGB patients has yet to be fully elucidated, fat malabsorption induced enteric hyperoxaluria likely plays an important role. Despite the absence of diarrhea, increased fecal fat is still noted after RYGB. Therefore, our meta-analysis confirmed an increased risk of kidney stones in patients following RYGB.

Purely restrictive bariatric procedures are not as effective as other weight loss (pure malabsorptive or mixed restrictive/malabsorptive) procedures. However, they do not cause hyperoxaluria. Although restrictive procedures may limit fluid intake, which may increase the risk of kidney stones, the effect of weight loss also reduces the risk of kidney stones. Thus, the findings of our meta-analysis successfully demonstrated an association between restrictive bypass surgery and a lower risk of kidney stones.

Although the data on the risk of kidney stones following mixed restrictive and malabsorptive procedures causing significant malabsorption such as very-long limb RYGB or biliopancreatic diversion with duodenal switch were limited, it has already been well established that these procedure can cause fat malabsorption which can lead to enteric hyperoxaluria and calcium oxalate stone formation. Recently, the findings from a population-based study by Lieske et al. reported an increased risk of kidney stones in patients following
malabsorptive procedures including very-long limb RYGB or biliopancreatic diversion/duodenal switch. In addition, the magnitude of kidney stone risk is high with HR of 4.15 (2.16–8.00).

Although almost all included studies were of moderate to high quality,14,15,17 there are some limitations. Firstly, there are statistical heterogeneities in the complete analysis of kidney stone risk in overall bariatric surgery. The potential sources of these heterogeneities include the differences in the diagnosis methodology of kidney stones and type of bariatric surgery. However, heterogeneities were insignificant to low with subgroup analysis of each type of bariatric surgery. In addition, there was only one included RCT16 in our meta-analysis. Although the meta-analysis of observational studies with adjusted analysis helps reduce bias due to observed covariates, a causal relationship needs to be cautiously interpreted. Also, the follow-up time for restrictive procedures in included studies was relatively short (2 to 4 years), not enough time to be certain that this procedure will not increase the risk of stones after four years, since impaired gastric acid secretion by lowering intestinal calcium absorption may facilitate intestinal oxalate absorption and thereby, raising urinary oxalate excretion as time passes.

In conclusion, our study demonstrates an association between RYGB and increased risk of kidney stones. Conversely, restrictive bariatric surgery may lower kidney stone risk. The findings in this study require future study with long-term follow-up to confirm this potential benefit of restrictive bariatric surgery.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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