### Kidney stones are common after bariatric surgery

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Obesity, a risk factor for kidney stones and chronic kidney disease (CKD), is effectively treated with bariatric surgery. However, it is unclear whether surgery alters stone or CKD risk. To determine this we studied 762 Olmsted County, Minnesota residents who underwent bariatric surgery and matched them with equally obese control individuals who did not undergo surgery. The majority of bariatric patients underwent standard Roux-en-Y gastric bypass (RYGB; 78%), with the remainder having more malabsorptive procedures (very long limb RYGB or biliopancreatic diversion/duodenal switch; 14%) or restrictive procedures (laparoscopic banding or sleeve gastrectomy; 7%). The mean age was 45 years with 80% being female. The mean preoperative body mass index (BMI) was 46.7 kg/m<sup>2</sup> for both cohorts. Rates of kidney stones were similar between surgery patients and controls at baseline, but new stone formation significantly increased in surgery patients (11.0%) compared with controls (4.3%) during 6.0 years of follow-up. After malabsorptive and standard surgery, the comorbidity-adjusted hazard ratio of incident stones was significantly increased to 4.15 and 2.13, respectively, but was not significantly changed for restrictive surgery. The risk of CKD significantly increased after the malabsorptive procedures (adjusted hazard ratio of 1.96). Thus, while RYGB and malabsorptive procedures are more effective for weight loss, both are associated with increased risk of stones, while malabsorptive procedures also increase CKD risk.

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Utilization of bariatric surgery continues to be high in the United States. Recent large, randomized trials confirm that patients have sustained weight loss, less mortality, and a decrease in obesity-related complications, such as diabetes, hypertension, and obstructive sleep apnea.<sup>1,2</sup> Thus, the number of bariatric procedures performed annually in the United States has increased from 12,775 to a peak of 135,985 in 2004; rates have since plateaued.

In 2008,  $\sim$  70% of bariatric procedures were Roux-en-Y gastric bypass (RYGB),<sup>3</sup> the preferred procedure, because it is associated with acceptably low morbidity and improved absolute and sustained weight loss compared with restrictive procedures (mainly adjustable gastric banding). Recently, sleeve gastrectomy has been reported to have an efficacy between that of gastric banding and RYGB.<sup>3</sup> Still RYGB is viewed as a more durable and effective procedure, especially in cases of severe obesity, and represented 56% of procedures in 2012.<sup>3</sup> The number of existing persons in the United States with RYGB procedures performed between 1998 and 2008 can be estimated to be ~830,000.<sup>4</sup> We previously reported a high incidence of hyperoxaluria and kidney stones among patients who had undergone RYGB for obesity.<sup>5</sup> Others have made similar observations in other patient cohorts.<sup>6-8</sup> The risk of hyperoxaluria and perhaps kidney stones may be less with other forms of bariatric surgery.9-i1 However, the risk for kidney stones and/or chronic kidney disease (CKD) with bariatric surgery remains unclear, because these studies were either not population-based or lacked controls with similar obesity and comorbidities who did not undergo bariatric surgery.

Thus, in the current study we used the resources of the Rochester Epidemiology Project<sup>12</sup> to conduct a populationbased study to compare the incidence of stones in patients after bariatric surgery with that in comorbidity-matched obese controls.

### RESULTS

There were 2683 patients with a history of bariatric surgery at Mayo Clinic during the study period. After excluding those without research authorization (n = 63), Olmsted County residency (n = 1832), or preoperative body mass index (BMI) greater than 35 kg/m<sup>2</sup> (n = 26), there were 762 bariatric

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#### Table 1 | Types of bariatric operations 2000–2011

	Malabsorptive procedure	RYGB	Restrictive	Other
Total number Number by year	105	591	56	7
2000–2003	43	127	0	0
2004–2007	36	273	15	1
2008–2011	26	191	41	6
Years of follow-up (mean (s.d.))	6.2 (3.7)	6.2 (3.1)	3.9 (1.6)	3.1 (2.6)
Age at surgery (mean (s.d.))	44.1 (11.0)	44.9 (11.2)	42.7 (12.0)	52.3 (9.3)
Sex (% female)	70.5%	82.9%	78.6%	57.1%
BMI kg/m <sup>2</sup> (mean (s.d.))	56.3 (8.4)	45.3 (6.5)	43.6 (7.6)	45.4 (10.0)

Abbreviations: BMI, body mass index; RYGB Roux-en-Y gastric bypass.

surgery patients to be studied. There were 13,256 Olmsted County residents with a BMI  $> 35 \text{ kg/m}^2$  during the study period. After excluding those who had undergone bariatric surgery (n = 699) and subjects who refused research authorization (n = 63), 12,494 potential controls remained. With 1:1 matching, we were able to identify controls for 759 of the 762 bariatric surgery patients.

Among the bariatric operations performed, most (n = 591), 78%) were standard RYGB procedures (Table 1). The majority of standard RYGB operations before 2007 were open procedures (n = 188), whereas laparoscopic procedures predominated after 2004 (n = 404). When a greater amount of weight loss was deemed desirable, procedures that were typically more malabsorptive in nature were performed, including very, very long limb RYGB (n = 55) or biliopancreatic diversion/duodenal switch (n = 50). At our institution, a relatively small number of restrictive procedures, including laparoscopic banding (n = 43) or laparoscopic sleeve gastrectomy (n = 13), were completed during the years of the study. The mean (s.d.) age at the time of bariatric surgery was 44.7 (11.2) years; 80% were female, and the mean preoperative BMI was 46.7(7.9) kg/m<sup>2</sup>; because of matching, these parameters were similar in controls (Table 2). Baseline comorbidities, including hypertension, diabetes, osteoarthritis, and sleep apnea, were more common in bariatric surgery patients than in obese controls (Table 2). CKD at baseline was similar between the two groups (10.4% vs. 8.7%; P = 0.26).

Nephrolithiasis at baseline had similar frequency in bariatric surgery patients and controls (4.0% vs. 4.2%; P = 0.70). In contrast, over a mean follow-up period of 6.0 (3.2) years, new (incident) stone events were found to be more common in bariatric surgery patients than in obese controls (11.1% vs. 4.3%; P < 0.01, Table 2). Kaplan–Meier plots confirmed that kidney stone events increased among operated patients within the first 2 years, reaching ~14% at 10 years compared with 7% of controls at that time point. Among the stones analyzed, calcium oxalate were the most common in bariatric patients before the procedure (73%)

Table 2	Demographics	of	bariatric	patients	and	controls
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	Bariatric patients (n = 759)	Controls ( <i>n</i> = 759)	P-value <sup>a</sup>
Demographics			
Age, years (mean, s.d.)	44.7 (11.2)	44.7 (11.2)	Matched
Female sex	80.6%	80.6%	Matched
BMI, kg/m <sup>2</sup> (mean, s.d.)	46.7 (7.9)	46.7 (7.8)	Matched
Years of follow-up	6.9 (3.4)	7.0 (3.3)	0.42
(mean, s.d.)		. ,	
Hypertension	52.3%	47.2%	0.05
Diabetes	27.1%	22.8%	0.05
Arthritis	56.1%	8.8%	< 0.001
Sleep apnea	56.8%	30.4%	< 0.001
CKD events			
Prevalence at baseline	10.4%	8.7%	0.26
New (incident)	7.9%	9.6%	0.24
Nephrolithiasis events			
Prevalence at baseline	4.3%	4.0%	0.70
New (incident) stones	11.1%	4.3%	< 0.01

Abbreviations: BMI, body mass index; CKD, chronic kidney disease.

<sup>a</sup>P-value from  $\chi^2$  test (nominal factors), rank sum test (continuous factors), and logrank test (time to incident CKD and stones).

Table 3 | Available stone composition of bariatric and obese patients, before and after the incident date

	Bariatric cohort		Obese cohort	
	Prevalent	Incident	Prevalent and incident	
Hydroxyapatite	3 (10%)	2 (3%)	7 (31%)	
Calcium oxalate	21 (73%)	63 (94%)	15 (65%)	
Struvite	2 (7%)	1 (1.5%)	1 (4%)	
Uric acid	3 (10%)	1 (1.5%)	0 (0%)	
Not available	4	17	40	

Values expressed as total number and % of those available.

and in obese control patients (65% before or after the incident date combined; Table 3). However, calcium oxalate stones were even more common after bariatric surgery, representing 94% of those analyzed (P = 0.02 for comparison of the stone distribution between the post-bariatric group and obese stone formers, using Fisher's exact test). Stone risk varied by type of procedure, being highest in patients who had undergone a malabsorptive procedure, intermediate in those who had undergone standard RYGB, and lowest in those who had undergone restrictive procedures, which were similar to the rates seen in obese controls (Figure 1). Baseline diabetes, osteoarthritis, sleep apnea, and being a bariatric surgery case were all significant risk factors for incident stones (Table 4). In multivariable models, only diabetes, RYGB, and malabsorptive procedures remained statistically significant risk factors. Patients with a history of a prior stone (prevalent) at the time of bariatric surgery were more likely to develop a stone after surgery compared with those without a prior stone history (42% vs. 14% at 10 years; hazard ratio = 4.1, P < 0.001). However, the risk of prevalent obese patients forming a second stone was slightly higher (52% at

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