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Bariatric surgery is associated with renal function improvement

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Abstract
Introduction Weight loss after bariatric surgery improves both blood pressure and glycemic control following surgery. The effect of bariatric surgery on renal function is not well characterized. In this study, we sought to quantify the change in renal function over time following surgery.
Methods We retrospectively reviewed all patients who underwent laparoscopic Roux-en-Y gastric bypass (LRYGB) or laparoscopic sleeve gastrectomy (LSG) between 2012 and 2014 at our institution. The glomerular filtration rate (GFR, mL/min) was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Body mass index (BMI, kg/m^2) and percent weight loss (%WL) were calculated following the surgery.
Results A total of 149 patients who underwent bariatric surgery were included in this study: LRYGB ($n = 86$ and LSG ($n = 63$). In LRYGB group, baseline BMI (kg/m^2, ±SD) and GFR (mL/min, ±SD) were 48.5 ± 6.8 and 94.7 ± 23.8, respectively. In comparison, BMI and GFR were 49.1 ± 11.9 kg/m^2 and 93.1 ± 28.0 mL/min in the LSG group, respectively. Over the follow-up period (19.89 ± 10.93 months), the patients who underwent LRGYB lost a larger percentage of weight as compared to those in the LSG group (29.9 ± 11.7% vs 22.3 ± 10.7%; $p = <0.0001$). Overall, GFR improved in both LRYGB (101.0 ± 25.8 mL/min) and LSG groups (97.9 ± 25.8 mL/min) and was not significantly different between the two groups. Of patients with a GFR < 90 mL/min prior to weight loss surgery ($n = 62$), 42% had improvement of their GFR to > 90 mL/min postoperatively ($p < 0.001$). There was no relationship between weight loss percentage and GFR improvement ($p = 0.8703$).
Conclusions Bariatric surgery was associated with improvement in postoperative renal function at almost two years following surgery but was not different for LRYGB versus LSG. The gain in GFR was independent of percentage of weight lost suggesting an alternate mechanism in the improvement of renal function other than weight loss alone.

Keywords Bariatric surgery · Renal function · Weight losss

Bariatric surgery has proven to be an effective agent in weight reduction and in treatment of both diabetes mellitus type 2 and hypertension [1, 2]. Obesity, diabetes, and hypertension are all independent risk factors in the development of chronic kidney disease (CKD). The hallmark of

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renal pathology observed in obesity is hyperfiltration and glomerulomegaly. Further, clinical evidence suggests that obesity accelerates the progression of underlying CKD [3]. Recently, focus has been centered on whether bariatric surgery can be utilized as a successful intervention in treating the kidney injury seen in obesity as suggested by some studies [4–7]. For instance, Serpa Neto et al. [8] evaluated the effect of weight loss after Roux-en-Y gastric bypass on renal function and blood pressure in 140 patients with morbid obesity and found that the GFR decreased from 150 to 115 mL/min 8 months after surgery. In another study of 61 patients, GFR and proteinuria improved 24 months after weight loss surgery [9]. Taken together, substantial weight loss after bariatric surgery is associated with reversing the hyperfiltration state seen in obesity. Accordingly, patients with obesity and some degree of mild renal dysfunction may represent a target population in whom bariatric surgery may help reduce CKD progression.

While laparoscopic Roux-en-Y gastric bypass (LRYGB) is considered the gold standard of bariatric surgery, laparoscopic sleeve gastrectomy (LSG) has emerged as the most commonly performed bariatric operation in the country [10, 11]. Both procedures are effective in terms of weight loss and improvement or remission of hyperglycemia or hypertension; however, LRYGB is associated with a greater amount of weight loss compared to LSG [12, 13]. The reasons for this are unclear, since the mechanisms of weight loss for both operations are not completely understood.

While there may be overlap in mechanisms of action, LRYGB and LSG may also act in different ways. We anticipated the effect on renal function would be different for each operation. Because LRYGB is associated with increased weight loss compared to LSG, we hypothesized that there would be a greater degree of improvement in postoperative renal function associated with LRYGB compared to LSG.

Materials and methods

After Institutional Review Board approval, an analysis of a prospectively maintained database was conducted for patients who underwent LRYGB and LSG from 2012 to 2014 at a single academic center. Exclusion criteria included open operations, revisional operations, as well as any patient who died within two years of their operation. Demographics were collected as well as preoperative and postoperative measures of height, weight, and the preoperative status of type 2 diabetes mellitus and hypertension. In addition, GFR measurements at non-bariatric physician appointments within the health system were collected for patients who did not attend the standard 8 postoperative bariatric appointments based on the electronic medical record.

Data were stratified by operation (LRYGB and LSG). After an initial post-surgical visit at 2 weeks, patients were eligible for eight bariatric follow-up appointments at three, six, nine, twelve, fifteen, eighteen, twenty-one, and twenty-four months. To account for variation in follow-up at each point, 45 days prior and 45 days following the expected time of clinic visit were considered at each time point. If a patient presented more than once during the same interval, only the outcome data from the visit nearest to the target date were included for analysis.

At bariatric clinic appointments, the patient's medication list is reviewed with them. At that time they are asked whether or not their primary care physicians are still prescribing diabetic or hypertension medications. Patients that denied being prescribed diabetic medications were determined to be in remission of diabetes. Likewise, patients that denied being prescribed hypertension medications at the time of follow-up visit were defined as being in remission of hypertension. GFR was calculated according to the CKD-EPI formula [14, 15]. The cohort was stratified by GFR < 90 or >90 mL/min. GFR was able to be obtained from the electronic medical record on all the patients in the study with laboratory data regardless of whether they attended postoperative bariatric clinic visits as they still received care within the institution. However, other variables including postoperative outcomes for weight loss and medications were not able to be reliably determined from the electronic medical record for those patients that did not return to follow-up in bariatric clinic.

Statistical analyses

Descriptive statistics were used to compare patient characteristics and compliance. Fisher's exact tests and Chi-square tests were used to compare categorical variable and Student's T test were used to compare differences between continuous variables, operation. Percent weight loss (%WL) and change in BMI (ΔBMI) were calculated for each. Multivariate linear regression was used to examine independent predictors of GFR improvement. Statistical analyses were conducted using SAS Version 9.4 (SAS Institute Inc. Cary, NC, USA) and R (Version 3.1.2, The R Development Core Team). Statistical significance was determined by $p < 0.05$.

Results

A total of 149 patients met criteria to be included in the study with 57% LRYGB ($n = 86$ and 43% LSG ($n = 63$) (Table 1). The majority of patients were female (84.6%).

Although there were no significant differences in the baseline characteristics of patients undergoing either surgical procedure, a higher rate of hypertension was observed in the LRYGB cohort as compared to LSG group (76.7 vs 63.5% $p = 0.06$). In the LRYGB group, baseline BMI and GFR were 48.5 ± 6.8 kg/m^2 and 94.7 ± 23.8 mL/min, respectively. In comparison, BMI and GFR were 49.0 ± 9.6 kg/m^2 and 93.1 ± 28.0 mL/min in the LSG group.

During the study period, 46 patients (30.8%) were lost to follow-up after their 3-month clinic visit and postoperative data were only available on 103 patients. The patients who underwent LRYGB had a higher %WL as compared to those in the LSG group (30.0 ± 11.7 vs 22.3 ± 10.7%, kg; $p = 0.001$). There was no significant difference regarding change in GFR or change in serum creatinine by operation (Table 1). There was no difference in postoperative outcomes regarding diabetes or hypertension remission in either group.

The population was then stratified based on the degree of preoperative kidney dysfunction as measured by GFR. Despite 46 patients not returning for all 8 bariatric surgery clinic visits, we did have GFR values on all 149 patients over the next 20 months from labwork available in the electronic medical record from other clinic appointments. Of patients with a GFR < 90 mL/min prior to weight loss surgery ($n = 62$), 42% had improvement of their GFR to >90 mL/min postoperatively ($p < 0.001$) (Table 2). The average GFR in this subset improved from 68.9 to 81.6 mL/min ($p < 0.0001$) and serum creatinine improved from 1.11 to 1.03 mg/dL ($p < 0.0001$). Overall, 26 patients did progress to worsening renal function after bariatric surgery and this correlated with significantly lower rates of hypertension remission (40.9 vs 49.2% $p = 0.006$) and lower rates of diabetes remission (54.6 vs 73.3%, $p = 0.073$) compared to those whose renal function improved postoperatively.

Changes in weight loss and GFR were plotted over time from surgery for both operations (Fig. 1). LRYGB had a significantly higher %WL over time compared to LSG (Fig. 1A) ($p < 0.001$). Despite the difference in trajectory of %WL by each operation, there was no difference in the improvement in postoperative GFR (Fig. 1B) ($p = 0.453$).

Table 1 Patient characteristics by operation

	Total ($N = 149$)	LRYGB ($N = 86$)	LSG ($N = 63$)	p value
Preoperative characteristics				
Age (years)	44.3 (10.9)	43.3 (10.4)	45.7 (11.6)	0.195
Sex (female)	126 (84.6)	72 (83.7)	54 (85.7)	0.740
Race (white)	81 (54.4)	45 (52.3)	36 (57.1)	0.560
Weight (lbs)	298.9 (67.4)	295.2 (52.9)	301.8 (84.6)	0.557
BMI (kg/m^2)	48.7 (9.1)	48.5 (6.8)	49 (11.9)	0.748
Hypertension	106 (71.1)	66 (76.7)	40 (63.5)	0.061
Serum glucose(mg/dL)	115.3 (41)	117.7 (44.2)	112.9 (38.9)	0.521
Diabetes	41 (27.5)	24 (27.9)	17 (27)	0.663
Serum creatinine (mg/dL)	0.895 (0.31)	0.893 (0.29)	0.9 (0.34)	0.893
GFR (mL/min)	93.9 (25.4)	94.7 (23.8)	93.1 (28)	0.704
Postoperative outcomes				
Number	103	62 (72.1)	41 (65.1)	0.512
Weight (lbs)	214.4 (56.3)	207.1 (57.1)	223.7 (51.9)	0.137
BMI (kg/m^2)	35.3 (7.9)	34.1 (8.2)	36.9 (7)	0.074
%WL	26.7 (11.9)	30 .0 (11.7)	22.3 (10.7)	0.001
ΔBMI	12.8 (5.9)	14.4 (5.7)	10.7 (5.6)	0.001
HTN remission	40 (37.7)	29 (43.9)	11 (27.5)	0.062
Serum glucose(mg/dL)*	100.2 (32.8)	106.2 (40.7)	92.9 (18.4)	0.012
Diabetes remission	28 (68.3)	16 (66.7)	12 (70.6)	0.952
Serum creatinine(mg/dL)	0.853 (0.43)	0.871 (0.53)	0.832 (0.271)	0.594
ΔSerum creatinine	−0.042 (0.36)	−0.02 (0.45)	−0.07 (0.216)	0.407
GFR (mL/min)	99.5 (24.9)	101.0 (25.8)	97.9 (25.1)	0.472
ΔGFR	5.6 (18.5)	6.29 (18.7)	4.86 (17.1)	0.634
Follow-up (days)	596.7 (327.8)	630.5 (347.8)	569.8 (297.8)	0.266

BMI body mass index; *%WL* percent weight loss; *GFR* glomerular filtration rate

* Data presented as *N* (%) or mean (SD); $p < 0.05$ considered significant

Table 2 Cohort stratified by glomerular filtration rate(mL/min)

Total patients	Total $N = 149$	GFR < 90 mL/min $N = 62$	GFR > 90 mL/min $N = 87$	p-value
Characteristics				
Age (Years)*		50.8 (9.1)	39.6 (9.8)	<0.001
Sex	Female	49 (79)	77 (89)	0.115
Race*	White	42 (68)	39 (45)	0.005
Surgery	LRYGB	35 (56)	51 (59)	0.792
	LSG	27 (44)	36 (41)	0.005
Weight (pounds)		297.8 (70)	298.2 (66.8)	0.972
BMI		48.4 (9.4)	49 (9.2)	0.698
GFR (mL/min)*		68.9 (15.6)	111.9 (13.3)	<0.001
Serum creatinine(mg/dL)*		1.11 90.36)	0.737 (0.12)	<0.001
Hypertension*		52 (83.9)	54 (62.1)	0.007
Diabetes*		23 (37.1)	18 (20.7)	0.016
Mean follow-up (days)		638.5 (352)	580 (308)	0.293
Postoperative outcomes				
Weight (pounds)		208.6 (52.2)	217.2 (57)	0.443
%WL		27.8 (12.4)	26.4 (11.6)	0.568
BMI		34.2 (6.8)	35.9 (8.4)	0.275
ΔBMI		13.5 (6.8)	12.6 (5.2)	0.443
GFR*(mL/min)		81.6 (24.5)	112.6 (16.9)	<0.001
ΔGFR*		12.7 (20.3)	0.68(14.3)	<0.001
GFR < 90 mL/min*		36 (58)	8 (9)	<0.001
GFR > 90 mL/min*		26 (42)	79 (91)	<0.001
Serum creatinine*(mg/dL)		1.03 (0.62)	0.728 (0.121)	<0.001
ΔSerum creatinine		−0.0871(0.55	−0.009 (0.1226)	0.279
Hypertension remission		16 (30.8)	24 (44.4)	0.058
Diabetes remission		17 (73.9)	11 (61.1)	0.059

GFR glomerular filtration rate; *BMI* body mass index; *SBP* systolic blood pressure; * denotes p-value < 0.05

Discussion

The aim of the current study was to evaluate the effect of weight loss after bariatric surgery on renal function (GFR) over 2 years of follow-up. We found that patients who underwent LRYGB had a modest but significantly greater %WL compared to LSG (30.0 vs 22.3%, $p = 0.001$). Further, GFR improved in both LRYGB (101.0 ± 25.8 mL/min) and LSG groups (97.9 ± 25.8 mL/min) during the follow-up period. However, this improvement in GFR was not statistically significant between the LRYGB and LSG groups. Interestingly, the improvement in GFR (expressed as change in GFR) occurred mainly in patients with a preoperative GFR < 90 mL/min as compared to those with GFR > 90 mL/min (12.7 ± 20.3 vs 0.68 ± 14.4; $p < 0.001$).

The finding that LRYGB is superior in terms of weight loss to LSG has been previously described in Maciejewski et al. in a study of the VA population that included 2,176 bariatric operations. Over a 4-year period, patients undergoing LRYGB lost 9.7% more weight than those undergoing LSG (95% CI, 0.8–18.6%) [12]. This is similar to our findings in which LRYGB lost 7.7% more weight compared to LSG. However, given these findings of superior weight loss with LRYGB, we found no difference by operation regarding the degree of improvement in GFR, suggesting that improvement in renal function after bariatric surgery is driven by other factors.

We found that bariatric surgery had a significant effect on improving GFR in patients with obesity and this effect was most dramatic in those with underlying kidney dysfunction (GFR < 90 mL/min). These findings are in concordance with those reported by Chun-Cheng Hou et al. [16] who evaluated the effect of bariatric surgery on renal function one year after surgery in 233 patients. They found a significant improvement in the mean GFR from 76.8 ± 16.7 mL/min to 93.3 ± 20.4 mL/min ($p < 0.05$) in the GFR 60–89 mL/min group and from 49.5 ± 6.6 to 66.8 ± 19.3 mL/min ($p < 0.05$) in the GFR 30–59 ml/min

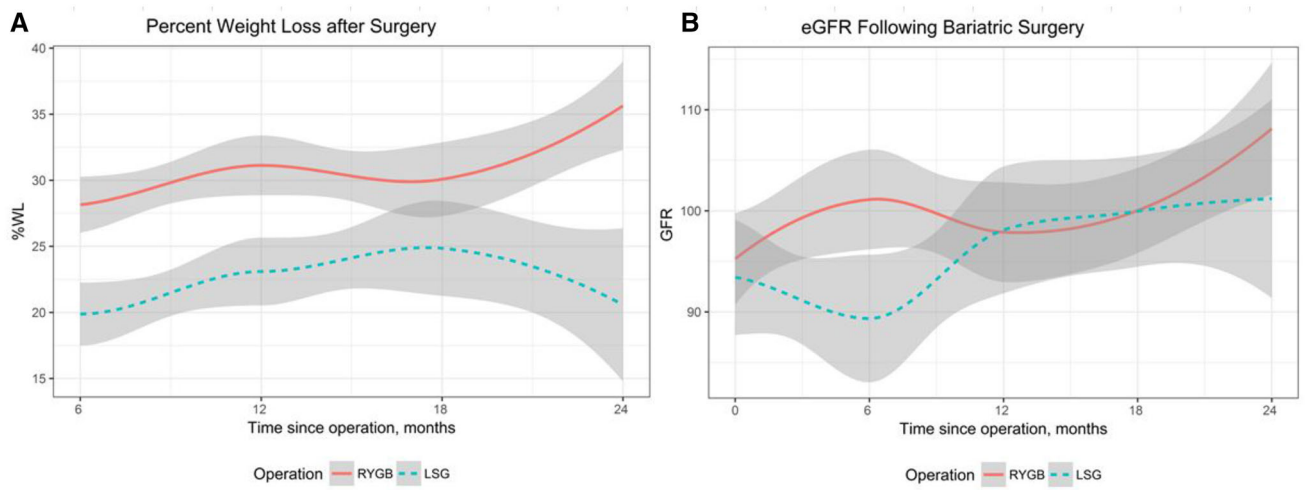

Fig. 1 **A** Smoothed plot of percent of weight loss in the 24 months following LRYGB and LSG patients. **B** Smoothed plot of calculated GFR(mL/min) in the 24 months following LRYGB and LSG patients

group. Since patients with obesity both with or without renal insufficiency demonstrate improved renal function after bariatric surgery suggests that bariatric surgery may be a plausible modality to treat, halt progression, or perhaps prevent CKD.

Insulin resistance and activation of the renin-angiotensin-aldosterone system leading to proteinuria and glomerulopathy have been identified as factors driving renal impairment in obesity [4, 17–19]. Numerous studies have found a link between improving renal function with weight loss and this has been thought to be driven by the remission of diabetes and hypertension. However, in our study, there was no significant difference in the remission of these comorbidities and improved GFR. For instance, a 2013 prospective study by Fenske et al. [20] found no difference in the degree of improved renal function when comparing laparoscopic adjustable gastric banding (LAGB), LRYGB, and LSG in 34 patients with obesity over a 12-month period. Interestingly, the authors found that each of the bariatric operations demonstrated a reduction in serum and urinary inflammatory markers that were directly correlated with weight loss. However, the patients undergoing LSG, LRYGB, and LAGB all had the same improvement in these systemic markers of inflammation over the study period. This observation suggests that a "threshold effect" exists for the weight loss following bariatric surgery and its effect on systemic inflammation and subsequent improvement in renal function [20]. This finding is also suggested in our graphic demonstration of improving GFR over time with both LRYGB and LSG despite a plateau effect on weight loss after surgery (Fig. 1). We speculate that bariatric surgery allows a threshold of weight reduction, which, in turn, could ameliorate the renal and systemic inflammation as well as the hyperfiltration state seen in obesity resulting in improving the hypertension and proteinuria.

Study limitations

Our study is limited by observational design and the potential for bias in which procedure selection and for those patients who were lost to follow-up. While many of the patients that were lost to follow-up ($n = 46$) within our bariatric clinic still sought care within our hospital system, the constraints of the electronic medical record did not allow for the reliable recording of variables including weight or medications and thus we were not able to report data on the entire cohort. Additionally, our study was based on a small sample size and is likely underpowered to detect other significant differences. It is our practice to defer the management of diabetic and anti-hypertensive medications to the primary care providers at our institution. Thus, our definition of diabetes and hypertension remission was based on patient reporting and not additionally verified with clinical and laboratory data. Currently, there is no validated method of measuring GFR in patients with rapid weight loss as lean muscle mass and creatinine also decrease during this period regardless of overall renal function. Additionally, we did not routinely collect urine samples during postoperative visits that would have allowed us to monitor proteinuria. Thus, our ability to make conclusions on the precise improvement in renal function is limited, but overall trends can be described.

Conclusion

Bariatric surgery is associated with improvement in postoperative renal function at 2 years following surgery,

especially in those patients with underlying kidney disease. While LRYGB was associated with a greater weight loss compared to LSG, the improvement in GFR over time was similar for both operations suggesting an alternate mechanism driving the improvement of renal function by bariatric surgery rather than weight loss alone.

Compliance with ethical standards

Disclosures Drs. Carla Holcomb, Lauren Goss, Amar Almehmi, Jayleen Grams, and Britney Corey have no conflicts of interest or financial ties to disclose.

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