ORIGINAL CONTRIBUTIONS





Comparative Effectiveness of Roux-en-Y Gastric Bypass vs. One Anastomosis Gastric Bypass on Kidney Function

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Received: 8 November 2020 / Revised: 9 February 2021 / Accepted: 10 February 2021 / Published online: 18 February 2021 © The Author(s), under exclusive licence to Springer Science+Business Media, LLC part of Springer Nature 2021

Abstract

Purpose Obesity and its associated medical problems increase risk of kidney function decline while prior studies suggest that bariatric surgery may improve kidney outcomes. However, little is known about the comparative effectiveness of different types of bariatric surgery on kidney function. In this study, we compare the effects of laparoscopic one anastomosis gastric bypass (LOAGB) and laparoscopic Roux-en-Y gastric bypass (LRYGB) on kidney function one year after surgery.

Materials and Methods The patients' demographic, medical, and surgical data were prospectively collected and retrospectively reviewed. Type 2 diabetes mellitus, hypertension, and dyslipidemia, body mass index (BMI), and kidney function tests were obtained before and one year after surgery. Kidney function was evaluated by estimated glomerular filtration rate (eGFR) and spot urine albumin to creatinine ratio (ACR). Changes in eGFR and ACR were compared between LRYGB vs. LOAGB after adjustment for confounders (age, sex, remission of associated medical problems, preoperative BMI, and percentage of excess BMI loss) using ANCOVA model.

Results Both surgical techniques significantly decreased the post-surgery presence of diabetes, hypertension, and dyslipidemia (p < 0.001 for all paired comparisons). The eGFR level significantly increased and the ACR level significantly decreased in both groups (p < 0.001 for all paired comparisons before and after adjustment). However, eGFR and ACR mean differences between LRYGB and LOAGB were not significantly different after adjustment for confounding variables (p = 0.9 and 0.4, respectively). **Conclusion** Both LOAGB and LRYGB improved 1-year eGFR and ACR equally independently from weight loss and other confounders.

Keywords Bariatric surgery · Gastric bypass · Albuminuria · Kidney · Creatinine

Introduction

Obesity is recognized as a global health crisis, currently impacting approximately one third of the world's population,

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cancer [3, 4]. While multiple studies demonstrate that obesity is an independent risk factor for chronic kidney disease (CKD) [6], this association may be less recognized by clinicians [7]. Potential pathophysiologic mechanisms include worsened hypertension (HTN) [8, 9], blood glucose, inflammation, dysregulation of adipocytokines, the autonomic nervous system, and the renin-angiotensin-aldosterone system [10, 11].

Bariatric surgery (BS) is now well-recognized as the most effective and sustainable method for substantial weight loss in patients with severe obesity [1–5]. Beyond weight loss, BS is very effective at inducing T2DM and HTN remission [8, 9, 12–14], as well as improving kidney function in patients with obesity-induced kidney dysfunction [6, 7, 10, 11, 14, 15]. Prior studies have found that BS prevents CKD in patients with normal kidney function while normalizing estimated glomerular filtration rate (eGFR) in BS candidates with hyperfiltration or decreased renal function category [14, 15]. The largest increase in eGFR appears to occur in those with lower baseline kidney function [10, 11, 15–19]. However, some kidney complications have been reported after BS, which are undeniable and associations between kidney function in and BS may differ by type of surgery [10, 11, 15–19].

Laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic one-anastomosis gastric bypass (LOAGB) are two types of gastric bypass surgeries with significant weight loss [13, 20-23]. Although LOAGB is newer than LRYGB, many studies have examined and compared the effects of LRYGB and LOAGB on weight loss, body mass index (BMI), and metabolic factors [13, 17, 19, 24-27]. It was observed that LOAGB patients may experience sharper trajectory of weight loss than LRYGB due to longer biliopancreatic limb (BPL), which may rarely cause malnutrition, liver failure, and kidney complications [28, 29]. It has been reported by meta-analysis and long-term studies that weight loss and T2DM remission rate after LOAGB are higher than LRYGB but remission of HTN was similar in both groups, which could impact future kidney function [26, 27, 30]. Non-inferiority analysis of the YOMEGA trial revealed that LRYGB is not inferior to LOAGB in terms of 2-year weight loss, and besides its 2-year missing data, complete and partial T2DM remission rate were 60% and 10%, respectively, in the LOAGB group vs. 38% and 6%, respectively, in the LRYGB group, although this finding was not statistically significant (p = 0.28) [13].

As there appear to be differences in metabolic effect between LOAGB and LRYGB, it remains unknown which surgical technique provides the best renoprotective effects [31]. Comparative effectiveness of LRYGB vs. sleeve gastrectomy (SG) [32] and LOAGB vs. SG [33] have been investigated in a few studies. No study has ever compared the effects of LOAGB vs. LRYGB on eGFR and albumin-creatinine ratio (ACR), and for each type of surgery, prior studies have incompletely adjusted for confounders or potential mediators such as remission of T2DM, HTN, or amount of weight loss [34]. Therefore, this study aimed to (1) compare the effects of LRYGB vs. LOAGB on eGFR and ACR one year after BS and (2) adjusted the kidney outcomes with potential mediating variables.

Materials and Methods

Design and Participants

This analysis used prospective cohort study of 2538 patients with severe obesity from 2015 to 2019. Their eligibility for BS were evaluated in the Isfahan University-affiliated Centers for Bariatric Surgery. Institutional review board certification was received before commencing this study and written informed consent was obtained from all patients before surgery. The 2016 IFSO Position Statements and 2012 Interdisciplinary European Guidelines on Metabolic and Bariatric Surgery and their later amendments were used as our surgical criteria [35]. Choosing the preferred surgical technique was based on patient willingness, preoperative evaluations, associated medical problems, and the surgeon's opinion. Detailed surgical procedures have been reported previously [28, 36-38]; however, in brief, for the LRYGB, a 7-10-cm gastric pouch with approximate volume of 30 cc, an alimentary limb of 60 cm, and a BPL of 130 cm were created, and for the LOAGB, a 18-20-cm gastric pouch with approximate volume of 50 cc and a gastrojejunal anastomosis 180 cm from Treitz ligament were created.

A total of 1986 patients underwent BS between January 2015 and December 2019 including 973 patients who underwent gastric bypass procedures. Patients were included in this study if they were aged 20-50 years, underwent either LRYGB or LOAGB for the first time, and had body mass index (BMI) 40–60 kg/m² or BMI 35–40 kg/m² with the presence of a obesity-associated medical problem (i.e., HTN and/ or T2DM). Exclusion criteria included history of other bariatric procedures, any history of kidney disease, nephrolithiasis, heart failure, pregnancy, malignancy, uncontrolled psychological disorders, preoperative eGFR below 60 milliliters per minute per 1.73 square meter as body surface area (mL/min/ 1.73 m^2), preoperative macroalbuminuria (ACR > 300 milligrams per gram (mg/g)), or incomplete clinical/ biochemical data. To decrease selection bias, patients were matched for age, sex, preoperative obesity-associated medical problems (HTN, T2DM, and dyslipidemia (DLP)), and baseline kidney function tests (eGFR and ACR).

A checklist including demographic data, type of the gastric bypass, presence of associated medical problems, and kidney function tests were obtained before and 12 months after the surgery. The percentage of excess BMI loss (%EBMIL) from 25 kg/m^2 was used as the weight-related variable for statistical analysis. A blood sample constituting fasting blood glucose,

lipid profile, creatinine (Cr), and a morning mid-stream urine sample were collected before and 12 months after the surgery.

American Diabetes Association 2015 report and its later amendments were used to diagnose, confirm, and define complete remission of T2DM [39]. The 2013 European Society of Hypertension and European Society of Cardiology report for HTN management and its later amendments were used to diagnose, confirm, manage, and define remission of HTN [40]. DLP was defined based on Adult Treatment Panel III cholesterol guideline [41].

The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula was used to calculate the eGFR [42]. Then, eGFR categories were defined as eGFR \geq 125 mL/min/1.73 m² as hyperfiltration (G0), 90 \leq eGFR \leq 124 as normal (G1), 60 \leq eGFR \leq 89 as decreased kidney function (G2), and eGFR \leq 59 as CKD (G3). ACR was measured in a morning mid-stream urine sample and its categories were defined as ACR < 30 mg/g as normal albumin excretion (A1) and 30 \leq ACR \leq 300 mg/g as microalbuminuria (A2) [19]. Improvement in eGFR and ACR were defined as coming to G1 category from another category and A2 to A1, respectively. Worsening in eGFR is when the postoperative eGFR was anything besides G1.

Statistical Analysis

Data was imported to the Statistical Package for Social Science (SPSS) software version 22.0 (IBM Corp., USA).

Table 1Participants'preoperative characteristics ineach group

Data were stratified by the gastric bypass type (LRYGB or LOAGB). Continuous and categorical data were presented as mean and standard deviation (SD) and frequency (percentage), respectively. The normality of continuous data was evaluated using the Kolmogorov-Smirnov test and the O-O plot, and non-normally distributed data were log-transformed. Categorical data were compared between groups using the chi-square test. Bonferroni correction was used and reported in case of finding significant difference. Paired t-test was used to compare before-after changes for each numerical variable in each surgical group. Analysis of covariance (ANCOVA) was used for comparing continuous variables when adjustment was made for confounding variables (i.e. age, sex, remission of T2DM, HTN, and DLP, preoperative BMI, and %EBMIL). The p value (two-tailed) < 0.05 was considered as a significant level.

Results

A total of 600 out of 851 LRYGB and LOAGB patients (300 patients for each group) fulfilled the inclusion/exclusion criteria. Participants' baseline characteristics are summarized in Table 1. No significant difference was observed between LRYGB and LOAGB groups.

Paired comparisons of each variable in either surgical groups are shown in Table 2. Although both surgical techniques significantly decreased the prevalence of T2DM, HTN, and DLP (all

		LRYGB $(n = 300)$	LOAGB $(n = 300)$	Р
Age (years)		40.15 ± 8.95	39.69 ± 11.06	0.77
Female, n (%)		252 (84)	252 (84)	0.58
Medical problems, <i>n</i> (%)	HTN	49 (16)	48 (16)	0.97
	DM	38 (13)	39 (13)	0.98
	DLP	174 (58)	175 (58)	0.28
BMI (kg/m ²)		43.68 ± 3.85	44.52 ± 6.43	0.6
eGFR level (ml/min/1.73m ²)		83.72 ± 18.30	83.36 ± 14.44	0.93
eGFR category, n (%)	G0 G1	9 (3) 90 (30)	5 (2) 82 (27)	0.78
	G2	201 (67)	213 (71)	
	G3	-	-	
ACR level (mg/g)		32.77 ± 22.81	30.66 ± 13.83	0.16
ACR category, n (%)	A1 A2	204 (68) 96 (32)	244 (81) 56 (19)	0.23

eGFR and ACR category definitions: G0: eGFR \geq 125 ml/min/1.73 m², G1: 90 \leq eGFR \leq 124 ml/min/1.73 m², G2: 60 \leq eGFR \leq 89 ml/min/1.73 m², G3: eGFR \leq 59 ml/min/1.73 m²; ACR: albumin-creatinine ratio, A1: ACR < 30 mg/g, A2: 30 \leq ACR < 300 mg/g

LRYGB laparoscopic Roux-en Y gastric bypass, *LOAGB* laparoscopic one-anastomosis gastric bypass, *n* number of patients, *HTN* hypertension, *DM* diabetes mellitus, *DLP* dyslipidemia, *BMI* body mass index, kg/m^2 kilograms per square meter, *eGFR* estimated glomerular filtration rate, $ml/min/1.73 m^2$ milliliter per minute per 1.73 of body surface area, *ACR* albumin-creatinine ratio, mg/g milligrams per gram

Table 2. Before-after comparisons of each variable in each gastric bypass group

		LRYGB $(n = 300)$			LOAGB $(n = 300)$		
		Before	After	Р	Before	After	Р
Medical problems, <i>n</i> (%)	HTN	49 (16)	16 (5)	< 0.001	48 (16)	5 (2)	< 0.001
	DM	38 (12)	7 (2)	< 0.001	39 (13)	20 (7)	< 0.001
	DLP	174 (58)	63 (21)	< 0.001	175 (58)	75 (25)	< 0.001
BMI (kg/m ²)		43.68 ± 3.85	30.03 ± 3.71	< 0.001	44.52 ± 6.43	29.88 ± 4.40	< 0.001
eGFR level (ml/min/1.73 m	²)	83.72 ± 18.30	93.00 ± 17.24	< 0.001*	83.36 ± 14.44	95.11 ± 15.88	< 0.001*
eGFR category, <i>n</i> (%)	G0 G1	9 (3) 90 (30)	10 (3) 169 (56)	0.01^{\dagger}	5 (2) 82 (27)	15 (5) 181 (60)	0.01^{\dagger}
	G2	201 (67)	116 (39)		213 (71)	103 (34)	
	G3	-	5 (2)		-	1 (0)	
ACR level (mg/g)		32.77 ± 22.81	16.11 ± 10.94	< 0.001*	30.66 ± 13.83	15.01 ± 12.52	< 0.001*
ACR category, n (%)	A1 A2	204 (68) 96 (32)	263 (88) 37 (12)	0.02 [‡]	244 (81) 56 (19)	276 (92) 24 (8)	0.02 [‡]

eGFR and ACR category definitions: G0: eGFR \ge 125 ml/min/1.73 m², G1: 90 \le eGFR \le 124 ml/min/1.73 m², G2: 60 \le eGFR \le 89 ml/min/1.73 m², G3: eGFR \le 59 ml/min/1.73 m²; ACR: albumin-creatinine ratio, A1: ACR < 30 mg/g, A2: 30 \le ACR < 300 mg/g

LRYGB laparoscopic Roux-en Y gastric bypass, *LOAGB* laparoscopic one-anastomosis gastric bypass, *n* number of patients, *HTN* hypertension, *DM* diabetes mellitus, *DLP* dyslipidemia, *BMI* body mass index, kg/m^2 kilograms per square meter, *eGFR* estimated glomerular filtration rate, ml/min/1.73 m^2 milliliter per minute per 1.73 of body surface area, *ACR* albumin-creatinine ratio, mg/g milligrams per gram

* *p* value both from paired *t*-test and ANCOVA model (adjustment was made for age, sex, remissions of comorbidities (hypertension, type 2 diabetes mellitus, and dyslipidemia), percentage of excess BMI loss, and preoperative BMI in each group)

[†] Bonferroni correction showed significant difference when comparing the G1 to either G0, G2, or G3 group

[‡]Bonferroni correction showed significant difference when comparing the A1 to A2

p values were < 0.001) (Table 2), T2DM remission was significantly higher in LRYGB (p = 0.01) and HTN remission was significantly higher in LOAGB (p = 0.015) (Table 3). BMI significantly decreased in both groups (p < 0.001) (Table 2); however, delta-BMI and percentage of EBMIL one year after surgery were not significantly different between two gastric by-passes (p = 0.49 and 0.27, respectively) (Table 3).

The eGFR level significantly increased and the ACR level significantly decreased in both groups (p < 0.001 for all paired comparisons before and after adjustment) (Table 2). Furthermore, the frequency of eGFR and ACR categories for each surgical group were significantly changed (Table 2). However, eGFR and ACR mean differences between LRYGB and LOAGB were not significantly different before (p = 0.18 and 0.21, respectively) and after adjustment for confounding variables (Table 3). The frequency of improvement/ no-change/worsening in eGFR and ACR was not significantly different between LRYGB and LOAGB (Table 3).

Discussion

The most important findings of this study were that (1) eGFR significantly increased and ACR significantly decreased after both types of gastric bypasses and (2) no significant difference was found between them before and after adjustment for

confounders. Therefore, both surgical techniques appeared to be equally effective in improving kidney function parameters independent from weight loss and remissions of associated medical problems.

LOAGB is nearly newer than LRYGB [13]; thus, prior studies in this field have focused primarily on the effects of LRYGB on kidney function [14, 43], have been limited by lack of data on changes in albuminuria, and often have not accounted for remission of hypertension and T2DM, which can impact kidney functions directly. For the first time, we report the effects of LOAGB on kidney function, showing similar beneficial effects on eGFR and ACR compared to LRYGB. This finding of improvement in albuminuria is important as albuminuria is a strong risk factor for future risk of cardiovascular disease and end-stage kidney disease. Studies have suggested that BS normalizes kidney function in patients with baseline hyperfiltration (G0) or with decrease eGFR (G2-G3) [6, 10, 17, 44]. Our findings confirm these observations and extend them to LOAGB.

Previous studies have found that the beneficial effect of BS on eGFR and albuminuria is explained by weight loss, lowering blood pressure, and T2DM remission [14, 16, 45–48]. Other studies suggest that improvements in albuminuria correlate with improvements in inflammation [16], and that improvements in eGFR correlate with improvements in leptin [49] and diastolic function [46]. In our study we also found

 Table 3. Associated medical

 problem remission rate, numerical

 variables' mean differences, and

 changes in qualitative definition

 of kidney function tests between

 two gastric bypasses

		LRYGB $(n = 300)$	LOAGB $(n = 300)$	Р
Remission rates, <i>n</i> (%)	HTN	33 (67)	43 (90)	0.015
	DM	31 (82)	19 (49)	0.01
	DLP	111 (64)	100 (57)	0.24
Delta-BMI (kg/m ²)		-13.65 ± 0.26	$-\ 14.63\pm 0.30$	0.49^{*}
EBMIL (%)		73.20 ± 18.94	74.55 ± 18.15	0.27
Delta-eGFR level (ml/min/1.73 m ²)		9.28 ± 1.21	11.74 ± 0.71	0.90^{*}
eGFR, $n (\%)^{\dagger}$	Improved No-change	107 (36) 158 (53)	116 (39) 162 (54)	0.67
	Worse	35 (12)	22 (7)	
Delta-ACR level (mg/g)		-16.66 ± 1.18	-15.65 ± 0.79	0.4^{*}
ACR, $n(\%)^{\dagger}$	Improved No-change	71 (24) 217 (72)	40 (13) 252 (84)	0.09
	Worse	12 (4)	8 (3)	

eGFR and ACR category definitions: G0: eGFR \geq 125 ml/min/1.73 m², G1: 90 \leq eGFR \leq 124 ml/min/1.73 m², G2: 60 \leq eGFR \leq 89 ml/min/1.73 m², G3: eGFR \leq 59 ml/min/1.73 m²; ACR: albumin-creatinine ratio, A1: ACR < 30 mg/g, A2: 30 \leq ACR < 300 mg/g

LRYGB laparoscopic Roux-en Y gastric bypass, *LOAGB* laparoscopic one-anastomosis gastric bypass, *n* number of patients, *HTN* hypertension, *DM* diabetes mellitus, *DLP* dyslipidemia, *BMI* body mass index, kg/m^2 kilograms per square meter, *EBMIL* excess BMI loss (assigning BMI = 25 as reference), *eGFR* estimated glomerular filtration rate, *ml/min/1.73* m² milliliter per minute per 1.73 of body surface area, *ACR* albumin-creatinine ratio, *mg/g* milligrams per gram

* *p* value from ANCOVA model. Adjustment was made for age, sex, remissions of comorbidities (hypertension, type 2 diabetes mellitus, and dyslipidemia), percentage of excess BMI loss, and preoperative BMI

[†] Improvement, worsening, or no-change in eGFR and ACR were defined based on their differences in distribution of each category (G0-G1-G2-G3 or A1-A2) between preoperative and postoperative

that the beneficial effects of LOAGB and LRYGB on the kidney were independent of changes in weight and remission of both HTN and T2DM.

It was revealed in some studies that LOAGB patients may experience higher weight loss [28, 29] and more T2DM remission than LRYGB [13, 26, 27, 30], which all together can impact the future kidney function. However, our findings did not support these hypothesis, which could be attributed to differences in our study population, differences in surgical technique, postoperative follow-up protocol, not including duration, severity, and control of associated medical problems (T2DM, HTN, or DLP), or other unknown factors. We did observe a trend towards greater %EBMIL and delta-BMI in LOAGB but there was no significant difference compared to LRYGB. T2DM remission was significantly higher in LRYGB and HTN remission was significantly higher in LOAGB. Although discrepancy in T2DM and HTN remissions may affect the changes in eGFR and ACR, kidney function improvement was distinct from remissions in associated medical problems similar to a study by Chang et al. [50].

Regarding the eGFR changes in other researches, 78% of the hyperfiltration group and 85% of the G3 group in Coupaye et al. study [10] and 63.2% of the hyperfiltration group and 82.4% of the G3 group in Magalhaes et al. study [17] had

kidney function improvement. Like these changes, 84.1% of the A2 group improve to A1 in Holcomb et al. study [6]. Altogether, BS can normalize the eGFR and ACR in patients with pathologic renal function and albuminuria; nevertheless, there are still some patients who do not benefit from this phenomenon, which needs more investigation [44, 51].

There were some limitations but also many strengths in our research. One limitation, similar to most surgical studies, is the lack of measured GFR. Albuminuria was only measured as a single ACR sample, although it is a valid variable; we recommend 24-h urine collection. A high proportion were females though this was similar in both groups and other bariatric surgery cohorts. We lacked long-term follow-up as renal function tests were obtained one year after the surgery; long-term follow-up might reveal different findings [21, 52]. Discrepancy in T2DM and HTN remissions between two groups may affect the way we concluded and analyzed eGFR and ACR. While we were able to adjust for many confounding variables, we did not include duration, severity, and control of associated medical problems as well as their consuming medications. Regardless, our study was strengthened by our large study sample size, the systematic capture of those associated medical problems, and including ACR, which is often missing in other studies. Findings provide important data supporting similar beneficial

effects of LOAGB and LRYGB techniques on kidney function, which have never been compared previously but needs more investigations and stronger analysis.

Conclusion

Although the severity and durations of associated medical problems were not captured and T2DM and HTN remissions were different between groups, both LOAGB and LRYGB can significantly and equally improve eGFR and albuminuria, independent of their beneficial effects on BMI, T2DM, HTN, and DLP.

Acknowledgments The authors express their gratitude toward Mr. Amir Salar Moazen Safaei for his kind support through this research.

Declarations

Ethical Considerations All procedures performed in this study were in accordance with the ethical standards of the institutional and national research committee and with 1964 Helsinki declarations and its later amendments. The study commenced after receiving its approval with the registration number of "IR.MUI.MED.REC.1397.223" from the Institutional Review Board of Isfahan University of Medical Sciences.

Informed Consent Informed consent was obtained before surgery from all individual participants included in the study.

Conflict of Interest All authors declare no potential conflict of interest.

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