

Impact of Weight Loss on the Severity of Albuminuria in Obese Diabetic Patients Undergoing Laparoscopic Sleeve Gastrectomy and One-Anastomosis Gastric Bypass

Ahmed Abdallah Salman¹, Mohamed Abdalla Salman², Mohamed H Aon¹, Reem Ezzat Mahdy³, Ahmed Abdallah², Gamal Galal Shemy⁴, Ahmed M Hassan⁴, Fatema Alzahraa Samy Amin⁵, Safa Labib¹

¹Internal Medicine Department, Faculty of Medicine, Cairo University, Cairo, Egypt; ²General Surgery Department, Faculty of Medicine, Cairo University, Cairo, Egypt; ³Internal Medicine Department, Faculty of Medicine, Assiut University, Assiut, Egypt; ⁴General Surgery Department, Faculty of Medicine, Al-Azhar University, Assiut Branch, Assiut, Egypt; ⁵Clinical Pathology Department, Faculty of Medicine, Cairo University, Cairo, Egypt

Correspondence: Ahmed Abdallah Salman, Internal Medicine Department, Faculty of Medicine, Cairo University, Cairo, Egypt, Tel +20 1000468664, Email awea84@kasralainy.edu.eg

Aim: To examine the effect of weight-loss induced bariatric procedures on albuminuria levels among diabetic patients suffering from obesity.

Methods: Adults patients who suffer from morbid obesity and type 2 diabetes mellitus (T2DM) were included in a prospective cohort study. Subjects were scheduled to undergo laparoscopic sleeve gastrectomy (LSG) or one-anastomosis gastric bypass (OAGB). The albumin-to-creatinine ratio (ACR) was adopted to assess the degree of albuminuria. Microalbuminuria was determined as a ratio of >2.5–30 mg/mmol and >3.5–30 mg/mmol for males and females, respectively, while macroalbuminuria was diagnosed when the ACR exceeded >30 mg/mmol.

Results: The mean uACR decreased significantly from 20.95±16.89 to 9.92±12.69mg/mmol in LSG cohort ($p < 0.001$), and from 19.52±16.65 to 9.34±11.77mg/mmol in the OAGB cohort, with no statistically considerable differences between both cohorts at the end of follow-up ($p = 0.78$). Twelve months after the procedures, the percentages of cases with microalbuminuria decreased significantly to 23.8% and 23.9%, respectively ($p < 0.001$); likewise, the percentages of cases with macroalbuminuria significantly decreased to 7.9% and 7.5% in the LSG and OAGB groups, respectively ($p < 0.001$). There were no statistically considerable differences between LSG and OAGB regarding the percentages of patients with micro or macroalbuminuria at the end of follow-up. Besides, there were no significant associations between the degree of weight loss and improvement ($p = 0.959$) or remission ($p = 0.73$) of microalbuminuria.

Conclusion: Bariatric surgery significantly reduced the severity of albuminuria 1-year after the procedure, with no preference for one procedure over the other.

Keywords: bariatric surgery, laparoscopic sleeve gastrectomy, one-anastomosis gastric bypass, microalbuminuria

Introduction

Diabetes (a term denotes coexistence of obesity and diabetes mellitus) is a growing global health concern with a progressive increase in its incidence in the Middle East and Africa.¹ The occurrence of type 2 diabetes mellitus (T2DM) is rising globally due to the sedentary behavior and high caloric density food that acts on susceptible genotypes.² On the other hand, the incidence of obesity has been tripled in the past few decades.³ While the interaction between T2DM and obesity is established, there are many uncertainties about the pathophysiological mechanisms underlying association. Obesity is a known contributor to insulin resistance and hyperglycemia through induction of chronic inflammation, dysfunctional entero-insular axis, and excessive release of adipokines.^{4,5} Regardless of the underlying

mechanism, the coexistence of obesity and T2DM significantly exacerbates the risk of various metabolic complications.⁶ Thus, recent guidelines emphasize the significance of weight loss on optimizing glycemic states in T2DM.⁷

Chronic kidney disease (CKD) is one of the most undesirable adverse effects of diabetes. Diabetic nephropathy is assumed to occur in nearly one-third of T2DM subjects, which, in return, can cause renal dysfunction and chronic renal failure.⁸ On the other hand, obesity alone represents an independent risk factor for CKD; excessive weight causes renal hyperfiltration and proteinuria, which consequently contributes to developing CKD.⁹ When obesity and diabetes co-exist, the risk of glomerulopathy, renal hypertension, and CKD increased progressively.¹⁰ Previous work showed that microalbuminuria, a well-recognized surrogate of renal dysfunction, is an early sign in obese patients with diabetic kidney disease; the magnitude of albuminuria was demonstrated to be considerably related to the body weight in diabetic patients suffering from obesity.¹¹ Furthermore, microalbuminuria was shown to be an early indicator of end-stage renal disease (ESRD) and cardiovascular comorbidities in these category of patients.⁹ Thus, it is logical to assume an improvement in the degree of albuminuria is a marker of resolution of obesity-mediated renal injury following any successful weight loss strategy.

Metabolic surgery, the most efficacious weight reduction approach, has a well-known effect on diabetes control in cases with T2DM.^{12,13} The improvement is mainly seen in the early postoperative period even before the weight loss is observed, and it is more obvious in patients who achieve the weight loss surgically than the non-surgical methods.^{14,15}

The physiopathological mechanisms that ameliorate glucose homeostasis following metabolic surgery are still unclear. Nonetheless, it is thought that the different gastrointestinal surgeries may have various effects and mechanisms of action. Bariatric surgery can help incorporate knowledge and multidisciplinary proficiency to supply a combination of conservative and surgical approaches for Type II diabetes. These treatments must be viewed as complementary choices and not alternative strategies, with the same aim of managing diabetes and attaining cure.¹⁶ In addition, a growing body of literature indicated a positive impact of weight reduction in post-bariatric renal functions, especially in diabetic patients.¹⁷

However, the effect of metabolic procedures on albuminuria, as an early predictor of progressive renal disease, has not been well studied yet. Therefore, the current work aimed to examine the effect of weight reduction following bariatric operations on albuminuria levels among diabetic patients suffering from obesity and to examine whether the type of surgery has a role in post-procedure albuminuria.

Subjects and Methods

Study Design and Population

In a prospective, observational study, adult cases (16–60 years old) who were scheduled to undergo laparoscopic sleeve gastrectomy (LSG) or one-anastomosis gastric bypass (OAGB) were recruited through the period from June 2014 to April 2018. Patients were deemed eligible if they had T2DM, a BMI >35 kg/m², and a history of resistance to conservative approaches for weight loss. The study complied with the Declaration of Helsinki.

Factors that were viewed when deciding on the type of operation to be done were preoperative BMI, existence of GERD, eating behavior, and point of view for every participant. Participants suffering from morbid obesity were advised that LSG should give inferior results compared to OAGB. Participants with GERD were advised about the possible refluxogenic adverse effect of LSG and the data results showing considerable resolution in reflux after OAGB.

American diabetes association (ADA) guidelines were adopted to define T2DM guided by fasting plasma glucose (FPG) concentration: clinical diabetes was determined as FPG ≥ 126 mg/dl or (glycosylated hemoglobin) HbA1c ≥ 6.5 , that was ensured by repeated blood samples unless the subject has clinical symptoms or glucose level of 200 mg/dl and previous history of the disease and/or usage of anti-diabetes drugs.¹⁸

We excluded patients with endocrinal causes for obesity, advanced medical conditions precluding anesthesia, not intending to modify lifestyle after operation, psychiatric contraindication, inconvenient social circumstances, previous bariatric operation, gestation, or lactation at screening or operation. All eligible cases signed written informed consent. The local ethical committee of Cairo University Hospitals approved the protocol.

Data Collection and Operational Definitions

Data were collected preoperatively then 1-year after the surgery. The data included demographic findings, history of chronic diseases, blood pressure, anthropometric measures, FPG, HbA1c, estimated glomerular filtration rate (eGFR), urine albumin-to-creatinine ratio (uACR), level of albuminuria, low-density lipoprotein (LDL), triglyceride, and cholesterol values.

The spot urine ACR measurements were adopted to evaluate albuminuria. The microalbuminuria was determined as an ACR of >2.5 – 30 mg/mmol and >3.5 – 30 mg/mmol for males and females, respectively. The macroalbuminuria was diagnosed when the ACR exceed >30 mg/mmol. The improvement in albuminuria was defined as any decrease in the levels of albuminuria. On the other hand, albuminuria cases, who had ACR of <2.5 mg/mmol at the end of follow-up, were defined as remitting cases.

The T2DM status at the end of follow-up was classified based on ADA; HbA1c lower than 5.7% with no diabetes drugs was viewed as remission and HbA1c 5.7–6.5% without diabetes drugs as partial remission.¹⁸

Surgical Technique

For patients who underwent LSG, pneumoperitoneum was induced using CO₂. The Harmonic Scalpel™ (Ethicon Endo-Surgery) was used to dissect the gastrocolic ligament. A 36-Fr orogastric tube was put into the stomach and adjusted towards the pylorus. The gastric resection was performed using a laparoscopic linear stapler. For cases submitted to OAGB, a 50 mL gastric pouch was created, and loop gastrojejunostomy was carried out 200 cm from Treitz ligament. We have implemented the Rutledge approach, but instead of transverse anastomosis, longitudinal gastrojejunostomy with 4.5 cm blue cartridge on the posterior aspect of the pouch has been adopted.

Study's Outcomes

The primary outcomes in this study were the change in mean uACR and the change in the percentages of cases with different grades of albuminuria at the end of follow-up. The secondary outcomes included the difference in the percentages of cases with different grades of albuminuria between LSG and OAGB groups, the changes in eGFR at the end of follow-up, the correlation between albuminuria changes and weight loss, the changes in blood glucose profile after 1 year, and the percentages of cases with improved or resolved T2DM at the end of the study.

Statistical Methodology

Statistical analysis was carried out through SPSS version 22. All variables were tested for distribution normality using Kolmogorov–Smirnov test. Based on data normality, mean \pm standard deviation (SD) or median (range) were utilized for the expression of continuous data. Categorical variables were expressed as numbers and percentages. The change between the baseline and follow-up period was examined using paired-*t*-test or Wilcoxon signed-rank test for continuous variables and McNemar test for categorical variables. The two groups were compared using independent *t*-test or Mann–Whitney test for continuous variables and Chi-square test for categorical variables. The *p* values were corrected with Bonferroni correction whenever indicated due to multiple comparisons. The rejection of the null hypothesis was stated when the *p*-value was <0.05 .

Results

A total of 130 subjects were included (LSG group = 63; OAGB group = 67). The mean age in the LSG cohort was 41.44 ± 7.81 years, and the majority were males (61.9%), while the mean age in the OAGB group was 41.75 ± 7.81 years ($p = 0.82$) and 62.7% were males ($p = 0.92$). The preoperative BMI was comparable between both groups ($42.92 \pm 4.03 \text{ kg/m}^2$ in the LSG group versus $41.88 \pm 3.45 \text{ kg/m}^2$ in the OAGB group; $p = 0.116$). Preoperatively, both LSG and OAGB had comparable values regarding history of smoking ($p = 0.694$), hypertension ($p = 0.486$), fasting blood glucose ($p = 0.417$), HbA1C ($p = 0.706$), and lipid profile ($p > 0.05$). The preoperative uACR was comparable between the LSG and OAGB groups (20.95 ± 16.89 versus $19.52 \pm 16.65 \text{ mg/mmol}$, respectively; $p = 0.628$). The preoperative data are shown in Table 1. Preoperatively, 41.3% and 41.8% of the patients had microalbuminuria in the LSG and OAGB groups, respectively, while 31.7% and 26.9% of cases had macroalbuminuria in the LSG and OAGB groups, respectively (Figure 1).

Table I Preoperative Data of the Examined Groups

Variables	LSG (n =63)	OAGB (n =67)	P value
Age (years)	41.44±7.81	41.75±7.81	0.826
Male	39 (61.9%)	42 (62.7%)	0.92
IHD	5 (7.9%)	6 (9%)	0.83
OSA	9 (14.3%)	9 (13.4%)	0.88
Height (cm)	169.98±6.77	169.28±7.89	0.589
Initial SBP (mmHg)	149.17±16.07	147.97±16.01	0.669
Initial DBP (mmHg)	93±12.77	93.84±12.98	0.712
Hypertension	33 (52.4%)	31 (46.3%)	0.48
Initial weight (kg)	128.22±10.16	126.88±12	0.495
Initial BMI (kg/m ²)	42.92±4.03	41.88±3.45	0.116
Initial fasting blood glucose (mg/dl)	151.51±40.48	157.4±41.95	0.417
Initial HbA1C (%)	7.29±1.18	7.22±1.06	0.706
Insulin therapy	18 (28.6%)	17 (25.4%)	0.68
OAD	49 (77.8%)	55 (82.1%)	0.53
Initial total cholesterol (mg/dl)	215.65±41.05	211.18±36.68	0.513
Initial LDL Cholesterol (mg/dl)	148.51±42.08	138.72±34.39	0.148
Initial HDL-Cholesterol (mg/dl)	52.25±7.89	54.84±7.32	0.055
Initial triglycerides (mg/dl)	198.11±31.59	196.19±32.05	0.732
Initial creatinine (mg/dl)	0.95±0.19	0.97±0.17	0.578
Initial uACR (mg/mmol)	20.95±16.89	19.52±16.65	0.628
Initial eGFR mL/min/1.73 m ²	91.81±7.2	92.21±7.47	0.757

Abbreviations: LSG, laparoscopic sleeve gastrectomy; OAGB, one-anastomosis gastric bypass; IHD, ischemic heart disease; OSA, obstructive sleep apnea; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; HbA1C, glycated hemoglobin; OAD, oral anti-diabetic; uACR, urine albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate. Data are presented as n (%) or mean±SD.

The mean uACR decreased significantly from 20.95±16.89 to 9.92±12.69mg/mmol in the LSG group ($p < 0.001$), and from 19.52±16.65 to 9.34±11.77mg/mmol in the OAGB group. The eGFR increased significantly in the OAGB group only ($p = 0.049$; [Table 2](#)).

Twelve months after the procedures, percentages of patients with microalbuminuria decreased substantially to 23.8% and 23.9%, respectively ($p < 0.001$); likewise, the percentages of patients with macroalbuminuria significantly decreased to 7.9% and 7.5% in the LSG and OAGB groups, respectively ($p < 0.001$; [Figure 1](#)).

There was no statistically considerable difference between LSG and OAGB regarding the percentages of patients with microalbuminuria after 12 months ($p = 0.961$). Almost 72% in the LSG had improved albuminuria, compared to 67.4% in the OAGB ($P = 0.650$), while 56.5% had remitting albuminuria in the LSG cohort, in comparison to 54.3% in the OAGB cohort ($p = 0.83$; [Figure 2](#)).

In addition, no significant associations were detected between percent of total weight loss and percentage of improved or remitting albuminuria ([Table 3](#)).

With regard to the changes in metabolic parameters, body weight, blood pressure, fasting blood sugar, HbA1C, and lipid profile decreased significantly after either LSG or OAGB ($p < 0.05$). The differences in these parameters

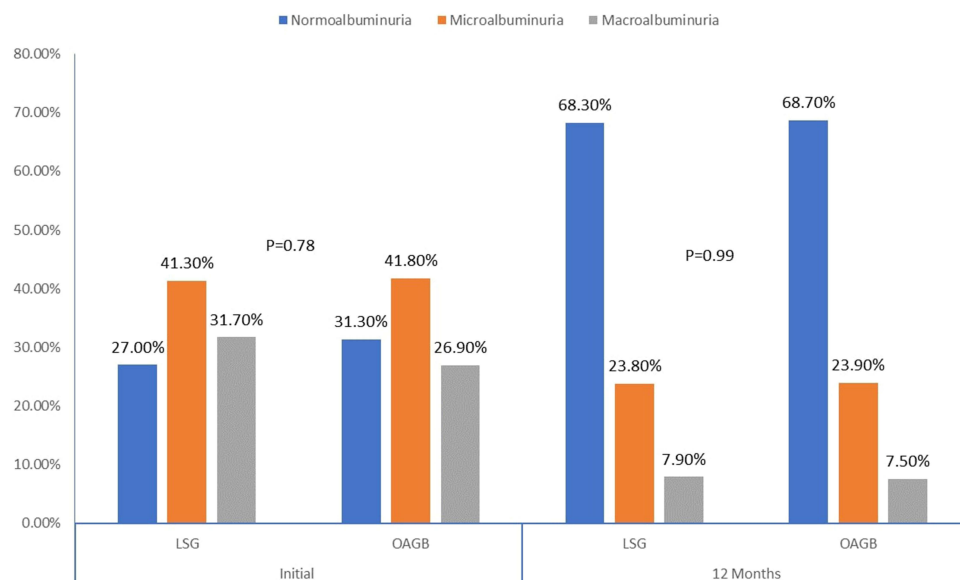


Figure 1 Percentages of patients with different classes of albuminuria pre and 1-year after the intervention.

between LSG and OAGB were not significant 1-year after the procedure ($p > 0.05$), except for HDL-cholesterol. The percentage of complete T2DM remission was 46% in the LSG cohort and 46.35% in the OAGB cohort ($p = 0.72$; Table 4).

Discussion

Few data are available regarding the effect of bariatric operations on the prevalence of post-procedure albuminuria, and whether one technique has superior results over the others in terms of the changes in the degree of albuminuria. In the current work, we compared different procedures (OAGB vs LSG) in terms of their effect on urinary albumin excretion. The choice of the operation for every participant was based on shared decision-making between the patient and the multidisciplinary team.

We demonstrated that bariatric surgery led to a statistically significant reduction in the degree of albuminuria among diabetic patients suffering from obesity. This reduction was consistent following LSG and OAGB, with no statistically significant difference. Similarly, previous studies failed in identifying differences between the effect of OAGB and LSG in terms of comorbidities improvement.¹⁹

On the other hand, no significant association was detected between the percent of total weight loss and the degree of albuminuria improvement.

Historically, eGFR was the marker of choice for progressive renal disease; however, eGFR is limited by being time-consuming with poor accuracy in detecting early renal damage.²⁰ Thus, over the past years, albuminuria has been viewed

Table 2 The Change in Renal Parameters in Each Group

	Baseline	LSG (n =63)		Baseline	OAGB (n =67)		P value
		After 12 Months	P value		After 12 Months	P value	
Creatinine (mg/dl) after	0.95±0.19	1.07±1.27	0.46	0.97±0.17	0.96±0.13	0.464	0.45
uACR (mg/mmol)	20.95±16.89	9.92±12.69	<0.001	19.52±16.65	9.34±11.77	<0.001	0.787
eGFR (mL/min/1.73 m²)	91.81±7.2	93.41±6.32	0.075	92.21±7.47	94.03±4.42	0.518	0.049*

Notes: *P value < 0.05 significant. Data are presented as mean±SD.

Abbreviations: LSG, laparoscopic sleeve gastrectomy; OAGB, one-anastomosis gastric bypass; uACR, urine albumin-to-creatinine ratio; eGFR, estimated glomerular filtration rate.

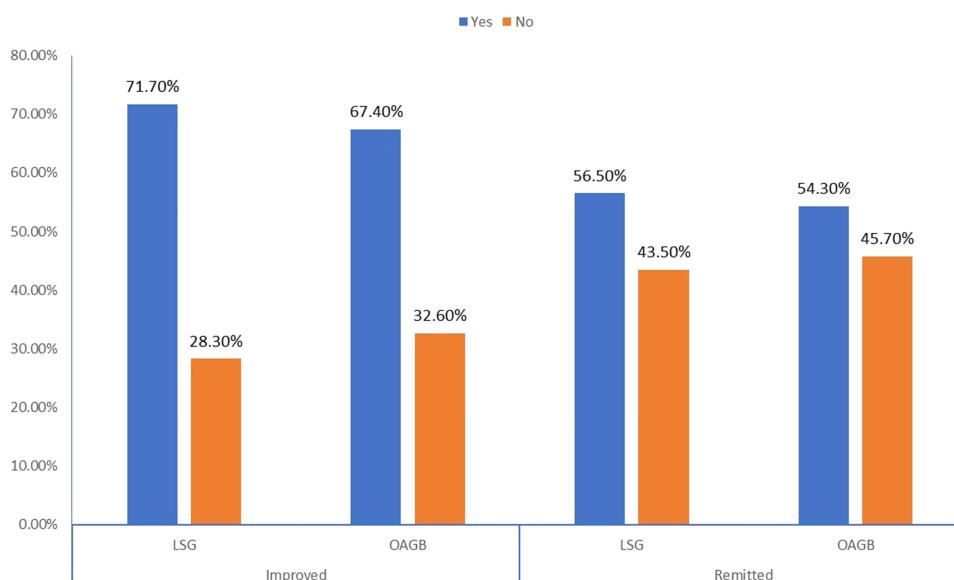


Figure 2 Percentages of improved and remitted albuminuria 1-year after the intervention.

as a reliable marker for renal damage in a variety of settings; microalbuminuria is an independent predictor for renal damage, progressive renal disease, acute renal failure, and ESRD.²¹ Moreover, microalbuminuria significantly predicts the risk of cardiovascular disease and death.²² Excess albumin excretion is prevalent in diabetic patients suffering from obesity owing to the synergistic adverse effect of both metabolic abnormalities on renal functions²³; the damage of glomerular filtration barrier due to hypertension and hyperglycemia, cytokines release from adipose tissue and increased intrabdominal pressure secondary to excessive visceral fat are among the many theories proposed for albuminuria development in diabetes.^{24,25} Previous reports demonstrated that microalbuminuria presents early in obese cases with diabetic nephropathy; the degree of albuminuria was found to be significantly correlated with body weight in diabetic patients suffering from obesity as well.¹¹ Thus, it is logical to assume an improvement in the degree of albuminuria should be a marker of the resolution of diabetes-mediated renal injury following any successful weight-loss strategy. In the present study, bariatric surgery resulted in a statistically substantial decline in the severity of albuminuria, with both techniques leading to a notable resolution. No significant association was found between weight loss and albuminuria.

In line with our results, Agrawal et al²⁶ demonstrated a considerable decrease in the prevalence of albuminuria 1-year after bariatric surgery, especially in diabetic patients. No significant correlation was found between albuminuria and degree of weight reduction in another retrospective study by the same author group.²⁷ Another two recent reports by Young et al²⁸ and Park et al²⁹ demonstrated a notable reduction in the microalbuminuria 1-year after bariatric operations in diabetic subjects with obesity. Notably, a 2015 report by Carlsson et al³⁰ demonstrated a lower incidence of

Table 3 Relation Between Total Weight Loss and Albuminuria Changes

		%TWL	p-value
Albuminuria improvement	Improved (n=55)	18.5±3.6	0.768
	Not improved (n=37)	18.2±4.6	
Albuminuria remission	Remission (n=36)	18.2±4.0	0.794
	No Remission (n=56)	18.5±4.1	

Note: Data are presented as mean±SD.

Abbreviation: TWL, total weight loss.

Table 4 The Change in Metabolic Parameters in Each Group

Variables		LSG (n =63)		OAGB (n =67)		P value
		12 Months	P value	12 Months	P value	
SBP (mmHg)		131.49±16.56	<0.001*	130.01±16.31	<0.001*	0.609
DBP (mmHg)		82.94±14.05	<0.001*	82.55±13.66	<0.001*	0.87
Cured hypertension		22 (73.3%)	< 0.001*	20 (71.4%)	< 0.001*	0.87
Weight (kg)		102.52±8.38	<0.001*	100.28±8.12	<0.001*	0.124
BMI (kg/m ²)		34.27±3.33	< 0.001*	33.72±3.15	< 0.001*	0.339
Weight loss (kg)		25.7±6.19		24.6±5.48		0.285
BMI change (kg/m ²)		8.65±2.15		8.16±1.64		0.145
Fasting blood glucose (mg/dl)		124.22±29.69	<0.001*	124.09±30.81	<0.001	0.980
HbA1C (%)		6.37±0.92	< 0.001*	6.42±0.86	<0.001*	0.744
DM	Partial remission	10 (15.9%)		8 (11.9%)		0.73
	Complete remission	29 (46%)		31 (46.35)		
	Non-remission	24 (38.1%)		28 (41.8%)		
Insulin therapy		7 (11.1%)	0.014*	8 (11.95)	0.046*	0.53
OAD		16 (25.4%)	<0.001*	23 (34.3%)	<0.001*	0.26
Total cholesterol (mg/dl)		182.9±35.28	<0.001*	181.81±34.47	<0.001*	0.858
LDL-cholesterol (mg/dl)		117.24±35.05	<0.001*	108.63±27.83	<0.001*	0.122
HDL-cholesterol (mg/dl)		55.62±9.26	<0.001*	59.63±9.83	<0.001*	0.018*
Triglycerides (mg/dl)		197.1±32.96	0.71	192.36±34.13	0.15	0.423

Notes: *P value < 0.05 significant. Data are presented as n (%) or mean±SD.

Abbreviations: LSG, laparoscopic sleeve gastrectomy; OAGB, one-anastomosis gastric bypass; SBP, systolic blood pressure; DBP, diastolic blood pressure; BMI, body mass index; DM, diabetes mellitus; HbA1C, glycated hemoglobin; OAD, oral anti-diabetic.

albuminuria in patients suffering from morbid obesity undergoing metabolic operations, in comparison to subjects suffering from obesity who receive conservative management.

Despite the notable effect of metabolic operations on the severity of albuminuria, the mechanisms of albuminuria improvement following the surgery are still largely unknown. The established reduction in the inflammatory status following bariatric surgery may explain albuminuria resolution, as detailed by Park et al²⁹ and others.^{31,32} Bariatric surgery resolves the obesity-induced inflammatory status, which can be subsequently associated with a reduction in the inflammatory insults towards the glomerular filtration barrier. The resolution of the lipotoxic effect of excessive adipose tissue and the glucotoxic effect of T2DM may represent a potential mechanism for albuminuria improvement following metabolic procedures.³³

The favorable effect of metabolic surgery on albuminuria was demonstrated in this analysis, the considerable decrease in the uACR 12 months postoperative. This was similar to a meta-analysis study performed by Upala et al,³⁴ in which a significant reduction in uACR was shown following metabolic operations. Moreover, Amor et al³⁵ and Henegan et al³⁶ reported an improvement of uACR after 1 year and 5 years of bariatric surgery, respectively.

A cumulative body of literature has established the beneficial role of metabolic operations on glycemic control among diabetic patients; previous reports indicated that bariatric surgery significantly improves the glycemic status and leads to diabetes remission in a considerable proportion of the patients.³⁷ In the present study, we found that both LSG and

OAGB led to a statistically significant reduction in the blood glucose and HbA1c 12 months after the operation; the percentage of complete T2DM remission was 46% in LSG group and 46.35% in OAGB group. These conclusions agree with recent meta-analysis studies that showed persistent improvement in glycemic control among patients who underwent bariatric surgery.^{38,39}

The current work may constitute a influential research in the future, given the novelty of the contribution and its clinically relevant value. Most importantly, given the statistical results, the study underlines the fact that bariatric surgeries have a favorable impact on albuminuria. Hence, this can strengthen the theory that the effects of metabolic operations are mainly metabolic and physiological rather than anatomical/mechanistic. Despite that, we admit that this work is limited by its observational nature that did not permit us to perform proper random allocation of the patients or blinding of the study's investigators. Also, the absence of the comparison with a group of patients who underwent conventional or intensive care of diabetes (no-surgery group) is another limitation.

In conclusion, bariatric surgery substantially cuts down the severity of albuminuria 1-year after the operation, with no preference for one over the other. This decrease was independent of the amount of weight loss. Future studies should examine the impact of the resolution of inflammatory markers, insulin resistance and hyperglycemia on the post-bariatric prevalence of albuminuria.

Novelty of the Work

Based on the published data, only a few reports have studied the changes in albuminuria after bariatric surgery. So this work adds a stream to the literature in terms of this novel topic. Besides, amongst the advantages of the current work is the reasonable number of cases in both groups with a fairly good follow-up period. This point may make our work quite singular as it is often not simple to get patients back for another look after 12 months.

Furthermore, it is plausible to say that this study may draw attention to potential mechanisms that may be driving the beneficial impact of metabolic procedures on the kidney and could provide promising horizons in terms of this aspect; and possibly make it an attractive goal for new therapeutic approaches in disorders related to obesity and kidney disease.

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Disclosure

The authors report no conflicts of interest in relation to this work.

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